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13. ABSTRACT ***(Maximum 200 Words)***

Extending work begun as part of a National Cancer Institute-funded project, we sought to determine whether variations in care received by older women affected short-term psychosocial and clinical outcomes. Our specific aims were: 1) To describe patterns of adjuvant hormonal and chemotherapy in older women, and factors associated with receipt of these therapies; 2) To characterize and quantify the breast cancer-related care received by older women during the early years following diagnosis; and 3) To determine the effects of ongoing breast cancer care on women's quality of life. We conducted a longitudinal observational study of 303 women ≥ 55 years of age diagnosed with stage I and II breast cancer between October 1992 and December 1995 at five sites in Boston, Massachusetts. Women were interviewed annually to obtain information about health and personal characteristics. Medical records were reviewed annually to gather information about treatments received, tests performed, and disease recurrences. We identified patient and provider characteristics associated with variations in care received and the effects of these variations on women's quality of life.

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Rebecca A. Sullivan 5/26/00

PI - Signature Date

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5. INTRODUCTION

Little is known about what constitutes appropriate care for older women with breast cancer (1) because until recently, women ≥ 70 years of age were excluded from most clinical trials. It is perhaps not surprising, therefore, that there continues to be considerable variation in how older women are treated (2-9). The current study was designed to identify determinants of variations in adjuvant hormonal/chemotherapy and follow-up care among older women with early stage breast cancer and the effects of these variations on health-related quality of life and breast cancer-specific function. As described in more detail below (**6. BODY**), we studied a cohort of women ≥ 55 years of age with newly diagnosed early stage breast cancer over a 4-year period. Baseline telephone interviews were conducted at 3-5 months following definitive primary tumor therapy, with subsequent interviews occurring approximately two years later, and annually thereafter for two years. Medical records were abstracted, beginning at the time of diagnosis and continuing until project completion, or the development of metastatic disease or subject death. The baseline interview and the medical record review covering the initial treatment period were funded by the National Cancer Institute. The follow-up interviews and medical record reviews were funded by the US Army Medical Research, Development, Acquisition and Logistics Command, the findings from which are described in this report.

We addressed the following **study questions** in the portion of the project funded by the US Army Medical Research, Development, Acquisition and Logistics Command:

1. What patient and provider characteristics are associated with the receipt of hormonal and/or chemotherapy?
2. What are the effects of hormonal treatment on patients' quality of life?
3. What patient and provider characteristics are associated with the receipt of surveillance tests?
4. What are the effects of surveillance testing on patients' quality of life?

Our **specific aims** were:

1. To describe patterns of adjuvant hormonal and chemotherapy in older women, and factors associated with receipt of these therapies.
2. To characterize and quantify the breast cancer-related care received by older women during the early years following diagnosis.
3. To determine the effects of ongoing breast cancer care (adjuvant therapy and disease surveillance) on patients' quality of life.

6. BODY

Overview and Findings from the Parent Study Funded by the National Cancer Institute (CA57754)

Funding from the National Cancer Institute (NCI) enabled us to enroll the cohort that was followed longitudinally for the current project. Patients ≥ 55 years of age with newly diagnosed early stage breast cancer, being cared for at one of five hospitals with academic affiliation in

Boston, Massachusetts, were enrolled between January 1993 and April 1996. Eligible patients were sent an introductory letter signed by their surgeon and a consent form approximately three months following initial surgical treatment. This was followed by a telephone call from our interviewer who further explained the study, answered questions, and obtained informed consent. Data were collected via a review of patients' surgical records, and a 30 minute computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included: histology, stage, estrogen receptor status, surgery performed, additional therapies received, and medical comorbidities. Our patient telephone interview included questions about: general health-related quality of life, breast cancer-specific quality of life, medical comorbidities, the treatment decision-making process, treatment priorities, perceptions of doctor-patient communication, and demographic characteristics.

Two papers published in 1997 and 1998 (10, 11) in ***Cancer*** summarized the methods and findings from the baseline data (see Appendix for reprints). Two related papers, but whose topics were not central to the specific aims of the original grant, were published in early 1999 (12, 13).

The first addressed upper-body function following primary tumor therapy:

RISK FACTORS FOR A DECLINE IN UPPER BODY FUNCTION FOLLOWING TREATMENT FOR EARLY STAGE BREAST CANCER (see Appendix for reprint)

Abstract

Purpose: To identify risk factors for a decline in upper body function following treatment for early stage breast cancer.

Methods: We conducted a cross-sectional observational study of 213 women ≥ 55 years of age newly diagnosed with early stage breast cancer interviewed three to five months following their definitive surgery. Patients were classified as having impaired upper body function related to their breast cancer treatment if: 1) they reported having no difficulty in performing any of three tasks requiring upper body function (pushing or pulling large objects; lifting objects weighing more than 10 pounds; and reaching or extending arms above shoulder level) prior to treatment, but reported that any of these tasks were *somewhat* or *very* difficult in the four weeks prior to interview, or 2) they reported that performing any of the three tasks requiring upper body function was *somewhat* difficult prior to treatment, but reported that any of these tasks were *very* difficult in the four weeks prior to interview.

Results: In multiple logistic regression models, both the extent and type of primary tumor therapy and cardiopulmonary comorbidity were significantly associated with a decline in upper body function following breast cancer treatment.

Conclusion: Given the critical importance of upper body function in maintaining independent living, clinicians should consider the functional consequences of treatment when they discuss treatment options and post-operative care with older women who have early stage breast cancer.

The second was a methodological paper that compares different strategies for measuring comorbidity:

COMPARISON OF INTERVIEW-BASED AND MEDICAL RECORD-BASED INDICES OF COMORBIDITY AMONG BREAST CANCER PATIENTS (see Appendix for reprint)

Abstract
Objectives: To compare patient interview-based and medical record-based measures of comorbidity and their relation to a range of patient outcomes, including primary tumor therapy and mortality, self-reported upper body function, and overall physical function.
Methods: 303 breast cancer patients age 55 years or older and diagnosed at 1 of 5 Boston hospitals were enrolled. Patient interviews and medical record abstracts provided the information necessary to construct the Charlson index, Satariano index, and a new interview-based index of cardiopulmonary comorbidity. These indices were used alone and in combination to predict the patient outcomes.
Results: The indices of comorbidity corresponded well with one another. The record-based Charlson index was the only index that predicted receipt of definitive therapy. No index of comorbidity predicted mortality over the short follow-up period. The new interview-based index of cardiopulmonary comorbidity was a better predictor of upper-body function and overall physical function than the interview-based or medical record-based Charlson or Satariano indices of comorbidity.
Conclusion: Older breast cancer patients are able to provide information about their diseases and related symptoms that correlates well with medical record-based measures of comorbidity and displays similar patterns of predictive power. A new self-reported measure of cardiopulmonary comorbidity performs better than the medical record-based measures for predicting patient-related functional outcomes.

Experimental Methods Used for Current Study

Institutional Review Board Approval: All annual Institutional Review Board approvals were obtained from each of the study sites. We received initial approval from Faulkner Hospital on November 14, 1995; from Boston Medical Center on November 15, 1995; from Boston City Hospital on December 27, 1995; from Beth Israel Hospital on October 16, 1995; and from New England Medical Center on December 12, 1995. Approvals were updated annually.

Study Implementation

Subject Enrollment and First Follow-up Interview in the Current Study. Subjects enrolled in the NCI study were mailed a consent packet 20 months after their diagnosis date. This time interval was chosen because it was the shortest interval possible between initial diagnosis and the initiation of the US Army Research, Development, Acquisition and Logistics Command funding.

The sample size available for study and the sample characteristics were constrained by the design and implementation of the parent NCI study. Specifically, although enrollment for the parent study was extended until April 1996, we did not achieve the sample size of 350 that we had originally planned. The number of participants was less than originally projected due to a smaller number of eligible patients from which to draw. This circumstance was due in part to the

departure from Boston of three well-known and established breast cancer surgeons. Non-participants were older (mean age=71.2 years for non-participants; mean age=68.4 years for participants), but there was no difference in the proportion of participants and non-participants with stage I and stage II disease. In addition, the original study was designed to compare younger postmenopausal women with older postmenopausal women. Two factors resulted in the youngest group of women (55-64 years of age) being the greatest contributors to our sample, and the oldest group of women (75+) being the smallest contributor. First, the number of women 55-64 years of age at risk for breast cancer is far greater than the number of women 75+ years of age at risk. Second, we, like all other investigators, experienced the highest refusal rate among the oldest group of women.

We completed data collection for the first follow-up interview in 1998. Of the 303 subjects who were eligible, 250 (83%) participated in this first follow-up interview. The reasons for non-participation included: 1) inability to contact – 30 (10%), 2) refusal – 16 (5%), 3) death – 5 (2%), and 4) too ill – 2 (1%).

Second Follow-up Interview. Our second follow-up interview took place approximately 12 months after the first follow-up interview. Data collection for this interview was completed in early 1999. A total of 225 subjects completed their second follow-up interview. This number reflects 215 subjects who participated in the baseline and first follow-up interviews and 10 who completed baseline interviews but could not be located for their first follow-up interviews. Of those who were eligible but not interviewed, 11 refused (this includes 6 who could not be located for their first follow-up interview but who, when located for their second follow-up interview, refused participation); 10 had died, 2 were too sick, and 24 who were unable to be located (this includes 5 who also could not be located for their first follow-up interview).

Third Follow-up Interview. Our third follow-up interview took place approximately 12 months after the second follow-up interview. Data collection for this interview was completed in December 1999. A total of 184 subjects completed this third interview. This included 3 subjects who did not complete their second follow-up interview. A total of 46 (20%) did not participate. Thirty could not be reached because residence and/or telephone numbers had changed. Eleven had died and 2 were too ill to participate. Three (1 %) refused to participate.

Collection of Surveillance Data. Medical record abstractions began in November 1994, and additional medical record abstractions were performed annually for each participant. To assess inter-rater reliability, a 20% random sample of charts were reviewed by Dr. Silliman. Medical record abstractions were completed for 247 of 250 (99%) subjects who completed the first follow-up interview. Two records were inaccessible because the patients had died and 1 patient received no further treatment or care. Abstractions were completed for 207 of 225 (92%) subjects who completed the second follow-up interview. Four records were inaccessible because the patients had died; 4 patients received no further treatment; 5 records could not be accessed because our original consent forms were considered to be out of date; and 5 records could not be located. Of the 184 subjects who completed the third follow-up interview, abstractions were completed for 160 (90%). Fourteen patients received no further treatment; 5 records could not be accessed because our original consent forms were considered to be out of date; and 5 records could not be located.

Results for Current Study

Study Question #1. What patient and provider characteristics are associated with the receipt of hormonal and/or chemotherapy?

Based on reviewers' comments about our manuscript addressing primary tumor therapy ("The Impact of Age, Marital Status, and Physician-Patient Interactions on the Care of Older Women with Breast Cancer"), we chose to address this question by analyzing the outcome according to the receipt of both primary tumor therapy as well as adjuvant systemic therapy. Thus, patients could be classified as yes/yes, yes/no, no/yes, and no/no. The manuscript was published in ***Medical Care*** in October 1999 (14).

THE CARE OF OLDER WOMEN WITH EARLY STAGE BREAST CANCER: WHAT IS THE ROLE OF SURGEON GENDER? (See Appendix for reprint)

Abstract

Background. - Over the past decade and a half a substantial literature has documented age-dependent variations in breast cancer care. Accumulating evidence suggests that these variations do impact the health outcomes of older women with breast cancer. Surgeon gender may be an important source of age-dependent variations in care.

Objective. - To examine the relationship between surgeon gender and primary tumor therapy and systemic adjuvant therapy among 303 older women with early stage breast cancer cared for by 20 surgeons in Boston, Massachusetts.

Research Design. - Cross-sectional observational study.

Subjects. - Women at least 55 years of age with newly diagnosed stage I or II breast cancer.

Main Outcome Measure. - Definitive primary tumor therapy and systemic adjuvant therapy.

Results. - After adjustment for patient and tumor characteristics, patients of female surgeons were more likely to receive definitive treatment, with the strongest effect being observed for the receipt of both definitive primary tumor therapy and systemic adjuvant therapy (OR 4.5; 95% CI 2.7, 7.7).

Conclusions. - Women with early stage breast cancer cared for by female surgeons are more likely to receive standard therapies. Surgeons provide the initial care for all women with breast cancer – both diagnostic as well as therapeutic care. Their role in breast cancer care is pivotal and has a substantial impact on the nature of breast cancer care received.

Study Question #2. What are the effects of hormonal treatment on patients' quality of life?

We took advantage of our longitudinal data (baseline, first follow-up interview, and second follow-up interview) to address several questions related to hormonal treatment, including this study question. A manuscript describing our approach and results was submitted to the ***Journal of Clinical Oncology*** in March 2000.

ADJUVANT TAMOXIFEN: PREDICTORS OF USE, SIDE EFFECTS, AND DISCONTINUATION IN OLDER WOMEN (see Appendix for a copy of the manuscript)

Abstract

Purpose: To identify predictors of adjuvant tamoxifen use, side effects, and discontinuation in older women.

Methods: We followed a cohort of 303 women 55 years of age or older diagnosed with stage I or stage II breast cancer for nearly three years following primary tumor therapy. Data were collected from women's surgical records and from computer-assisted telephone interviews at 5, 21, and 33 months following primary tumor therapy.

Results: Two hundred and ninety-two of the 303 (96%) patients in the study provided information about tamoxifen use. Tamoxifen use was reported by 189 (65%) patients; 26 (15%) discontinued use during the follow-up period. Being older (65-74 vs. 55-64 years of age), having stage II disease, being estrogen receptor positive, seeing a greater number of breast cancer physicians, and having better perceptions of one's abilities to discuss treatment options with physicians were associated with a greater odds of tamoxifen use. Better physical function, having received standard primary tumor therapy, and having obtained helpful breast cancer information from books or magazines were associated with lesser odds of tamoxifen use. The oldest patients (75+ years) [relative to youngest old (55-64 years)] and patients with better emotional health had significantly lesser odds of reporting side effects. Patients who were estrogen receptor positive were less likely to stop taking tamoxifen; patients who experienced side effects were more likely to stop taking tamoxifen.

Conclusions: Deviations from a prescribed course of adjuvant tamoxifen occur relatively frequently. The clinical consequences of this deviation need to be identified and quantified.

Study Question #3. What patient and provider characteristics are associated with the receipt of surveillance tests?

As noted above, medical record abstractions were completed for 247 of 250 (99%) subjects who completed the first follow-up interview; 207 of 225 (92%) subjects who completed the second follow-up interview; and 160 of 184 (90%) subjects who completed the third follow-up interview. The surveillance period was defined as beginning three months after the completion of definitive primary tumor therapy. This definition could mean, for example, three months after a modified radical mastectomy, three months after the completion of radiation therapy following breast conserving surgery, or three months after the completion of systemic adjuvant chemotherapy. If a patient developed a recurrence, we defined surveillance as not being reinitiated until three months after completion of therapy for the recurrence. We reviewed records to determine whether and how often the following surveillance tests were obtained by surgeons, radiation oncologists, and medical oncologists: medical history, physical examination, mammography, blood tests (complete blood count [CBC], liver function studies [LFTs], and carcinoembryonic antigen [CEA]), and other radiologic studies (chest x-ray, skeletal survey, bone scan, and liver scan). We did not include tests that were performed because of patients' symptoms. Across all types of surveillance tests, the number of tests obtained during the follow-up period ranged from 0 to 64.

During the follow-up period, office visits for breast cancer surveillance that included a medical history and physical examination occurred most often. Over the entire follow-up period, the average number of these office visits were as follows: surgeons – 5.5 (maximum=14); radiation oncologists – 3.6 (maximum=12); and medical oncologists – 4.5 (maximum=12). Among these cancer specialists combined, the average total number of visits was 10.3 (maximum=25). Also among these specialists, the annual average number of visits for a medical history and physical examination was: Year 1 – 2.8 (range = 0-10); Year 2 – 3.0 (range = 0-8); Year 3 – 2.7 (range = 0-9); and Year 4 - 2.2 (range = 0-9). Postmenopausal women with early stage breast cancer were seen frequently by all three types of cancer specialists and the number of visits per year remained about the same until the fourth year of follow-up.

The average number of surveillance mammograms obtained by all cancer specialists combined was 3.9 (maximum=9). Surgeons averaged 3.2, followed by radiation oncologists who averaged 1.15, and medical oncologists who averaged 0.6. Over the follow-up period, women averaged about one mammogram per year (range = 0 – 4 per year). Other radiologic studies were obtained infrequently. Surveillance blood tests were obtained more frequently, and primarily by medical oncologists. All three types of hematologic studies were obtained up to five times per year for each of the first three years of follow-up, and up to three (CEAs) or four (CBCs and LFTs) during the fourth year of follow-up.

We conducted logistic regression analyses to examine the relationship between patient characteristics and two surveillance test outcomes: any mammography and any blood work over the follow-up period. With mammography as the dependent variable and controlling for the type of primary tumor therapy received (*e.g.*, mastectomy or breast conserving surgery plus radiation therapy), older women (75+ years of age) had a lesser odds of having received surveillance mammography (OR = 0.32, 95% CI 0.15-0.66) compared to younger women. Additional analyses did not indicate that education, comorbidity, or stage differences were explanations for the age effect. Similarly, with blood work as the dependent variable and controlling for the receipt of systemic adjuvant therapy (*e.g.*, chemo- or tamoxifen therapy), older women (75+) also had a lesser odds of having received surveillance blood tests (OR = 0.39, 95% CI 0.15-1.01) compared to younger women. These data suggest that the oldest women with early stage breast cancer may receive too few surveillance mammograms and that younger postmenopausal women may receive too many blood tests.

A manuscript reporting these results is in preparation.

Study Question #4. What are the effects of surveillance testing on patients' quality of life?

The primary quality of life outcome variables of interest for this analysis were changes in physical function, general emotional health, and breast cancer-specific emotional health. The physical function and general emotional health measures are subscales of the SF-36 (16). We developed breast cancer-specific emotional health measure and have described it previously (11). To describe changes in these variables over the follow-up period, we dichotomized them to indicate "higher" (favorable) or "lower" (unfavorable) status. We applied formal cluster analysis to create dichotomous variables (high/low) for physical function and general emotional health. For the high/low classifications of physical function, "higher" physical function may be

interpreted as "*not limited at all*", on average, to questions regarding limitations to perform activities on a typical day (responses = *limited a lot, limited a little, and not limited at all*). "Higher" general emotional health may also be interpreted as "*all of the time*" or "most of the time" responses, on average, to questions such as "Felt full of pep?" and "Had a lot of energy?" (responses = *a little, some, a good bit, most, and all of the time*). For breast cancer-specific emotional health we used a cutoff point so that the "higher" status reflects, on average, "*excellent*" or "*very good*" responses to questions regarding a subject's ability to deal with breast cancer worries (responses = *poor, fair, good, very good, and excellent*).

Based on the high/low classification, four types of transitions between baseline and the second follow-up interview were defined: high-to-high, low-to-high, high-to-low, and low-to-low transition. For simplicity and clinical relevancy, the first two groups were combined to reflect a favorable transition and the latter two groups were combined to reflect an unfavorable transition. Our independent variables included age, marital status, comorbidity, therapies received, doctor-patient communication, and the number of surveillance tests received.

To explore the crude associations between categorical and continuous variables we used two-sample t-tests (or analysis of variance) and for associations between categorical variables we used chi-square tests of proportions (or Fisher's Exact-test when needed). The association between changes in each quality of life measure and the explanatory variables was evaluated using logistic regression models.

Physical Function:

At baseline 83%, 75%, and 67% had "higher" scores on physical function, general emotional health and breast cancer specific emotional health. At baseline about 83% of the patients had "higher" (favorable) physical function scores. The majority (79%) had a favorable transition between baseline and the second follow-up interview, while 21% had an unfavorable transition in physical function. The multiple logistic regression analysis results are shown in the table on the following page.

Logistic Regression Model Predicting Change in Physical Function

Variable	β Coefficient	Odds Ratio (95% CI)
Age		
55 – 64	---- Referent ----	
65 – 74	0.36	1.44 (0.58, 3.58)
75+	1.82	6.16 (1.99, 19.07)
Comorbidity		
0	---- Referent ----	
1 – 3	1.15	3.17 (1.30, 7.73)
4+	1.99	7.30 (2.81, 18.96)
Primary Tumor Therapy	-0.16	0.88 (0.33, 2.20)
Surveillance Testing	0.01	1.01 (0.98, 1.04)

Older age and a higher comorbidity score were significantly associated with an unfavorable transition in physical function. Women who were 75 years of age or older had about 6.2 times greater odds of having an unfavorable transition over the follow up period compared to the youngest group women. Similarly, patients who had more cardiopulmonary comorbidity at baseline were more likely to have an unfavorable transition in physical function (OR=7.3 and OR=3.2 for patients with two levels of cardiopulmonary comorbidity, compared to those who had no cardiopulmonary comorbidity). Surveillance testing was not associated with either a favorable or an unfavorable transition in physical function.

General Emotional Health:

At baseline about 75% of the patients had "higher" (favorable) general emotional health scores. The majority (74%) had favorable transition and 26% had an unfavorable transition in general emotional health. The multiple logistic regression analysis results are shown in the table on the following page.

Logistic Regression Model Predicting Change in General Emotional Health

Variable	β Coefficient	Odds Ratio (95% CI)
Age		
55 – 64	---- Referent ----	
65 – 74	-0.58	0.56 (0.25, 1.27)
75+	-0.76	0.45 (0.15, 1.48)
Marital Status	-0.87	0.42 (0.20, 0.87)
Comorbidity		
0	---- Referent ----	
1 – 3	0.32	1.38 (0.59, 3.24)
4+	1.27	3.56 (1.41, 8.98)
Tamoxifen Use		
Stopped	---- Referent ----	
Never Took	-0.88	0.42 (0.14, 1.26)
Still Taking	-1.15	0.32 (0.11, 0.91)
Primary Tumor Therapy	-0.55	0.58 (0.22, 1.48)
Ability to Communicate	-0.98	0.38 (0.13, 1.06)
Rating of Physician Technical And Interpersonal Care	-0.58	0.56 (0.26, 1.22)
Surveillance Testing	-0.02	0.98 (0.95, 1.00)

Patients with more cardiopulmonary comorbidity had significantly greater odds of having an unfavorable transition in emotional health when compared to patients with no cardiopulmonary comorbidity (OR=3.6). On the other hand, married patients and those who were continuing to take tamoxifen had significantly lower odds of having an unfavorable transition, when compared to unmarried patients and patients who stopped taking tamoxifen (OR=0.4, p=0.02; and OR=0.3, p=0.03, respectively). Variables that were of borderline statistical significance were one the patient-doctor interaction indicators as well as surveillance testing. Patients who were better able to communicate with their physicians (OR=0.4; p=0.07), and those who had more surveillance testing (OR=0.98; p=0.08) were more likely to have a favorable transition in general emotional health.

Breast Cancer-Specific Emotional Health

At baseline about 67% of the patients had "higher" (favorable) breast cancer specific emotional health scores. Unlike the transitions in physical function and general emotional health, a smaller proportion (only 61%) had a favorable transition and a greater proportion (39%) had an unfavorable transition in breast cancer-specific emotional health. The multiple logistic regression analysis results are shown in the table below.

Logistic Regression Model Predicting Breast Cancer-Specific Emotional Health

Variable	β Coefficient	Odds Ratio (95% CI)
Age		
55 – 64		---- Referent ----
65 – 74	-0.26	0.77 (0.37, 1.63)
75+	-1.89	0.15 (0.04, 0.51)
Marital Status	-0.27	0.76 (0.39, 1.50)
Comorbidity		
0		---- Referent ----
1 – 3	1.03	2.79 (1.28, 6.06)
4+	1.58	4.87 (1.88, 12.62)
Primary Tumor Therapy	-0.16	0.85 (0.33, 2.15)
Chemotherapy	-1.02	0.36 (0.13, 0.97)
Ability to Communicate	-0.99	0.37 (0.15, 0.92)
Rating of Physician Technical and Interpersonal Care	-1.53	0.22 (0.10, 0.46)
Surveillance Testing	-0.01	0.99 (0.97, 1.01)

Older patients (75 years of age or older), those who received chemotherapy, those who were better able to communicate with their physician, and those who rated their physician's skills as "excellent" had favorable breast cancer-specific emotional health transitions (all $p<0.05$). On the other hand, patients with higher cardiopulmonary comorbidity scores had significantly greater odds of having an unfavorable transition (OR=4.9 and OR=2.8 for the two higher levels of cardiopulmonary comorbidity, compared to women who had no

cardiopulmonary comorbidity). Surveillance testing was not related to either favorable or unfavorable transitions in breast cancer-specific emotional health.

Taken together, these data do not provide evidence that surveillance testing has a substantial impact on the quality of life of older breast cancer survivors over a three year period of time. A manuscript reporting these results is in preparation.

Additional Analyses

1. Upper Body Function

In addition to addressing Study Question #2 above by taking advantage of the longitudinal nature of our data, we have examined the relationship between patient characteristics and treatments and a decline in upper body function, as well as the relationship between patient characteristics and changes in quality of life over the first three years of follow-up. This manuscript will be published in June 2000 in the *Journal of Clinical Epidemiology* (15).

PATIENT CHARACTERISTICS AND TREATMENTS ASSOCIATED WITH A DECLINE IN UPPER-BODY FUNCTION FOLLOWING BREAST CANCER THERAPY (see Appendix for a copy of the manuscript)

Abstract
Breast cancer therapy is often followed by a decline in upper-body function. 303 women diagnosed with Stage I or II breast cancer were interviewed 5 and 21 months after surgery and their medical records were reviewed. Women with cardiopulmonary comorbidity had an odds ratio for decline at the 5 month interview of 2.8 (95 percent CI 1.3-5.7), relative to women without. Women who received mastectomy (OR = 2.5; 95 percent CI 0.9-6.7) or breast conserving surgery with radiation therapy (OR = 2.9; 95 percent CI 1.0-8.9) were at higher risk for decline at the 5 month interview than women who received only breast conserving surgery. Women who had axillary dissection were more likely to report numbness or pain in the axilla (OR = 6.4; 95 percent CI 1.2-33) at the 21 month interview than women who did not. Clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with women who have early stage breast cancer.

2. Mortality

We have obtained information regarding deaths from physicians, families, and local newspaper obituaries. Twenty-seven subjects have died (9%). We have obtained death certificates for 23 of these from the Massachusetts Department of Vital Records. Fifteen (65%) died of breast cancer and 8 (35%) died of other causes. To more comprehensively obtain information on patient deaths we submitted an application to the US Department of Health and Human Services in May 1999 for use of the National Death Index (NDI). Because of the time lag in updating of information in the NDI (1998 data will not be available until January 2000), the time period covered was 1993-1998. The small number of total deaths limits our ability to conduct valid analyses. To overcome this problem, we have combined our data with data

collected by Dr. Silliman and colleagues in Rhode Island. One of our doctoral students, Aliza Fink, received the Boston University School of Public Health prize for the best student abstract presented at the Boston University Science Day, March 29, 2000. The abstract is below.

5-YEAR SURVIVAL OF WOMEN TREATED WITH BREAST CONSERVING SURGERY AND RADIATION THERAPY COMPARED TO WOMEN RECEIVING A TOTAL MASTECTOMY

AK Fink, TL Lash and RA Silliman (Departments of Epidemiology and Biostatistics and Medicine)

The National Surgical Adjuvant Breast and Bowel Project Protocol B-06 – a randomized clinical trial comparing breast conserving surgery and radiation therapy to total mastectomy in women with early stage breast cancer – found that over five years of follow-up 76% of those receiving a total mastectomy survived compared to 86% of those receiving breast conserving surgery and radiation therapy ($p = 0.07$). The objectives of our analysis are to determine whether a similar pattern is observed in a clinical practice setting, whether there are time trends in type of treatment received between 1984–86 to 1992–5.

We pooled data from two observational cohort studies of women who were aged 45 or older (56% were 65 or older) with local or regional disease. The first study included 357 women diagnosed with breast cancer between July 1984 and February 1986 at one of eight Rhode Island hospitals. The second study included 265 women diagnosed with breast cancer between October 1992 and December 1995 at one of five hospitals in Boston, Massachusetts. Medical records provided information on type of surgery and potential confounders (*e.g.* age, stage and comorbidity). All women included in this analysis were treated with either a total mastectomy or breast conserving surgery with radiation therapy. The follow-up period was five years. Information on death due to breast cancer and all cause mortality was ascertained from the National Death Index. The data were analyzed using Cox's proportional hazards regression. The propensity score method also was used to adjust for potential confounding because it simulates randomization.

During 1984–6, 16% of women received breast conserving surgery with radiation therapy compared to 73% during 1992–5. 72.4% of women who were treated with a mastectomy survived the 5 years after surgery compared to 86.0% of women treated with breast conserving surgery and radiation therapy, representing a 14% greater survival. Women treated with a total mastectomy were twice as likely to die of any cause during the 5-year follow up than women treated with breast conserving surgery and radiation therapy (relative hazard = 2.0; 95% CI 1.2–3.2). Similarly, women treated with a total mastectomy experienced a 2.6-fold increase in breast cancer deaths compared to those treated with breast conserving surgery and radiation therapy (relative hazard = 2.6; 95% CI 1.2–5.5).

This analysis suggests, similar to the randomized trial, that 5-year survival is improved among women treated with breast conserving surgery and radiation compared with those treated with total mastectomy.

7. KEY RESEARCH ACCOMPLISHMENTS – see 8. REPORTABLE OUTCOMES

8. REPORTABLE OUTCOMES

Manuscripts, Abstracts, and Presentations

a. Dr. Silliman was invited to write an editorial as a companion to an article on age-related treatment variations published in the Journal of the National Cancer Institute June 4, 1996. Silliman RA. Breast cancer care in older age: Where do we go from here?

b. Six research reports have been published.

1) Silliman RA, Troyan SL, Guadagnoli E, Kaplan SH, Greenfield S. The impact of age, marital status, and physician-patient interactions on the care of older women with breast cancer. Cancer 1997; 80:1326-34.

2) Silliman RA, Dukes KA, Sullivan LM, Kaplan SH. Breast cancer care in older women: Sources of information, social support, and emotional health outcomes. Cancer 1998; 81:706-11.

3) Silliman RA, Prout MN, Field T, Kalish SC, Colton T. Risk factors for a decline in upper body function following therapy for early stage breast cancer. Breast Cancer Research and Treatment 1999;54:25-30.

4) Silliman RA, Lash TL. Comparison of interview-based and medical record-based indices of comorbidity among breast cancer patients. Med Care 1999;37:339-49.

5) Silliman RA, Demissie S, Troyan SL. The care of older women with early stage breast cancer: What is the role of surgeon gender? Med Care 1999;37:1057-67.

6) Lash TL, Silliman RA. Patient characteristics and treatments associated with a decline in upper body function following breast cancer therapy. J Clin Epid 2000; *in press*.

c. Another manuscript has been submitted for publication:

1) Demissie S, Silliman RA, Lash TL. Adjuvant tamoxifen: Predictors of use, side effects, and discontinuation in older women. J Clin Oncol; *under review*.

d. Dr. Silliman has co-authored three book chapters with Dr. Lodovico Balducci:

1) Balducci L, Silliman RA, Baekey P. Breast cancer: An oncological perspective - Part I. In: Balducci L, Lyman GH, Ershler WB, eds. Comprehensive Geriatric Oncology. Australia:Harwood Academic Publishers, 1998:629-660.

2) Silliman RA, Balducci L. Breast cancer: A geriatric perspective - Part II. In: Balducci L, Lyman GH, Ershler WB, eds. Comprehensive Geriatric Oncology. Australia:Harwood Academic Publishers, 1998:661-664.

3) Silliman RA, Balducci L. Breast cancer. In: Gallo JJ, Busby-Whitehead J, Rabins PV, Silliman RA, Murphy JB, eds. Reichel's Care of the Elderly: Clinical Aspects of Aging (5th ed). Baltimore: Williams & Wilkins, 1999:407-413.

e. Ms. Fink, a doctoral student of Dr. Silliman received the Boston University School of Public Health prize for the best student abstract presented at the Boston University Science Day, March 29, 2000. It is entitled "5-year survival of women treated with breast conserving surgery and radiation therapy compared to women receiving a total mastectomy."

f. Dr. Silliman was invited to speak at the Cancer in the Elderly 1996 Conference (November 1996), at a lecture series sponsored by the Massachusetts Department of Health (January 1997), at a special meeting of medical oncology educators in Puerto Rico (February 1997), and at a conference convened by the National Institute on Aging and the National Cancer Institute to address comorbidity measurement in older cancer patients (July 1999).

g. Dr. Silliman was invited to participate in a two and one-half day retreat to assist the National Cancer Institute's Breast Cancer Progress Review Group (September 1997) in developing a breast cancer research agenda for the next five years.

Funding Applied for Based on Work Supported by this Award

Dr. Silliman (Principal Investigator) and colleagues submitted a grant proposal to the National Cancer Institute June 1, 1995 entitled "Adjuvant Tamoxifen Therapy in Old Age: Determinants and Consequences" (R01 CA/AG 70818). It was funded and began September 30, 1996. The current project is much smaller in scope but provided important preliminary data for the new project. This new project is examining patterns of adjuvant tamoxifen prescribing patterns in much more detail and enrolled patients $\geq$ 65 years of age at four sites (Los Angeles, Minnesota, Rhode Island, and North Carolina). A total of 765 women have been enrolled in this study. About half are $\geq$ 75 years of age. A follow-up proposal entitled "Breast Cancer Treatment Outcomes in Older Women" (RO1 CA84506) was submitted to the National Cancer Institute February 1, 1999. Again, the current project provided important preliminary data. The project has been approved for funding; with a scheduled award date of June 1, 2000.

9. CONCLUSIONS

Older women's age, aspects of social support, and doctor-patient interactions are predictive of both how they are treated and their quality of life outcomes. Studies are needed that can more definitively determine whether variations in treatments received are associated with variations in recurrence and mortality outcomes. For example, is less than standard care associated with poorer outcomes? Such studies are particularly critical given the continued poor track record of recruiting older women into clinical trials (17). In this regard, efforts to design clinical trials specifically for older women with breast cancer need to be supported as should interventions designed to enhance recruitment into such trials. Finally, should studies find that less than standard care is associated with poorer outcomes, interventions then need to be

developed that target both systems as well as clinician and patient factors that are associated with the receipt of less than standard care.

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11. APPENDIX

REPRINTS OF PUBLISHED RESEARCH REPORTS

COPIES OF MANUSCRIPTS *IN PRESS* OR *UNDER REVIEW*

BIBLIOGRAPHY

LISTING OF PERSONNEL RECEIVING PAY FROM THE RESEARCH EFFORT

Aging and Cancer

Cancer special section

The Impact of Age, Marital Status, and Physician-Patient Interactions on the Care of Older Women with Breast Carcinoma

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Understanding why older women with breast carcinoma do not receive definitive treatment is critical if disparities in mortality between younger and older women are to be reduced. With this in mind, the authors studied 302 women age ≥55 years with early stage breast carcinoma. Data were collected from surgical records and in telephone interviews with the women. The main outcome was receipt of definitive primary tumor therapy, defined either as modified radical mastectomy or as breast-conserving surgery with axillary dissection followed by radiation therapy. The majority (56%) of the women underwent breast-conserving surgery and axillary dissection followed by radiation therapy. After statistical control for four variables (comorbidity, physical function, tumor size, and lymph node status), patients' ages, marital status, and the number of times breast carcinoma specialists discussed treatment options were significantly associated with the receipt of definitive primary tumor therapy. The authors concluded that when older women have been newly diagnosed with breast carcinoma and there is clinical uncertainty as to the most appropriate therapies, patients may be better served if they are offered choices from among definitive therapies. In discussing therapies with them, physicians must be sensitive to their fears and concerns about the monetary costs and functional consequences of treatment in relation to the expected benefits. ***Cancer* 1997;80:1326–34.** © *1997 American Cancer Society.*

The cumulative risk for breast carcinoma reaches its maximum well into the ninth decade of life. Almost half of all newly diagnosed breast carcinomas occur in women who are age 65 years or older.[1] Although older women are less likely to die of their breast carcinoma than younger women,[2] recent evidence suggests that older women who do not receive definitive primary tumor therapy are at greater risk of dying from the disease than older women who do receive definitive therapy.[3] This finding is particularly important because older women are also at greater risk of not receiving definitive treatment than younger women.[4–12]

Understanding the reasons why older women do not receive definitive treatment, particularly if the receipt of such treatment results in poorer patient outcomes, is critical if we are to improve such outcomes. Previous investigations have evaluated the potential roles of patients' health status (comorbidity and functional status);[6,8,11] patients' preferences and their families' preferences and support;[13,14] and aspects of patient-physician interactions (physicians' attitudes and beliefs[8,15] and the adequacy of patient-physician communication[16]) in explaining age-related treatment variations. For example, when tumor characteristics are taken into account, comorbidity and functional status do not completely explain the tendency of older

women to receive less-than-definitive treatment.[6,8,11] In addition, married women are more likely to receive definitive therapy than their unmarried counterparts.[10,13] Finally, physicians who report a greater willingness to involve patients in treatment decision-making tend to be those who recommend breast-conserving surgery without regard to age.[15]

In addition to the well-known association, particularly among women, between older age and being unmarried and less-than-definitive therapy,[17] recent literature has documented that the quality of physician-patient interactions decreases with patient age. Physicians tend to spend less time with their older patients than with their younger patients and be less respectful towards their older patients than towards their younger patients. For their part, older patients tend to be less assertive and defer more to their physicians for treatment decisions than their younger counterparts.[18] Whether these features of patient-physician interactions represent cohort effects that will disappear with subsequent generations of physicians and patients is not known. For the present, however, they remain.

Because previous studies of age-related variations in the care of patients with breast carcinoma have not evaluated comprehensively the extent to which patients' ages, marital status, health status (comorbidity and functional status), tumor characteristics, and aspects of physician-patient interactions are independently associated with treatments received, we studied older women newly diagnosed with early stage breast carcinoma and identified factors associated with the receipt of definitive primary tumor therapy. We chose age 55 years as the lower boundary of age eligibility to have a group with which to compare the younger old (ages 65–74 years) and the older old (age 75+ years) age groups. We used a conservative definition of definitive primary tumor therapy (modified radical mastectomy or breast-conserving surgery with axillary dissection followed by radiation therapy), recognizing that there are no specific guidelines for the care of older women with early stage breast carcinoma.

METHODS

Sampling

Women age ≥55 years newly diagnosed with histologically confirmed Stage I or II invasive breast carcinoma who had no previous history of other kinds of cancer within the previous 5 years, had no previous history of breast carcinoma, and were cared for at 1 of 5 hospitals with academic affiliation in Boston, Massachusetts, were eligible for study.

To identify potentially eligible patients, project staff reviewed pathology reports at each participating hospital on a regular basis, beginning in October 1992 and ending in December 1995. Names of potentially eligible patients were faxed to participating surgeons, who confirmed eligibility and also indicated if there were any patients that they did not want us to contact and the reason for this decision. Eligible patients were sent an introductory letter signed by their surgeon and a consent form approximately 2–3 months after initial surgical treatment. This was followed by a telephone call from our interviewer, who further explained the study, answered questions, and obtained informed consent.

Data Collection and Instrumentation

Data were collected via a review of patients' surgical records and a computer-assisted telephone interview with consenting eligible patients.

Medical record abstract

Data collected from medical records included: histology (infiltrating ductal, infiltrating lobular, medullary, mucinous/colloid, or tubular), tumor size (largest diameter of the sum of the largest diameter of all fragments), stage (TNM), estrogen receptor status (positive or negative, according to each laboratory's reference values), the results of axillary dissection if performed, breast surgery performed (mastectomy or breast-conserving surgery), and additional therapies received (radiation therapy, chemotherapy, and/or hormonal therapy). Because the performance of axillary dissection is related to age and we were particularly interested in patterns of care related to age, we chose not to exclude patients who could not be staged based on axillary lymph node pathology. Such women were staged clinically.

Medical records were monitored for 6 months after surgery to determine whether radiation therapy and chemotherapy were initiated and completed, and whether hormonal therapy was initiated. All medical record information was collected by two trained research assistants. A 20% random sample of records abstracted by each research assistant was rereviewed by the other as well as by one of us (R.A.S.). Item interrater reliabilities ranged from 88% to 100%, with most discrepancies occurring early in the study.

Patient interview

The patient telephone interview was conducted an average of 4.5 months after definitive surgery and took 35 minutes to complete. It included questions about demographic characteristics (age, race, marital status, living arrangements, education, employment, and income); cardiopulmonary comorbidity and functional status; factors important in breast carcinoma treat-

ment decision-making, including goals of therapy, side effects of treatment, recommendations of physicians, recommendations of family and friends, and cost; and perceptions of doctor-patient communication. All interviews were conducted by one experienced interviewer.

Major Analytic Variables

Our main outcome variable was definitive primary tumor therapy, defined either as modified radical mastectomy or as breast-conserving surgery with axillary dissection followed by radiation therapy, versus all other primary therapies received (e.g., breast-conserving surgery without radiation therapy).

For our independent variables, we considered variables from four categories. First, we considered demographic characteristics, including age (categorized as ages 55–64, 65–74, and 75+ years, to allow for comparisons among those in late middle age, the younger old, and the older old), marital status (married/not married), and education (<high school/ ≥high school). We did not include income because of the large amount of missing data (24% of subjects did not provide income information).

Second, we considered two measures of health status, because comorbidity and functional status have been shown to contribute unique information to the understanding of the health of older persons.[19,20] We assessed comorbidity using a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, ischemic heart disease, and related disease manifestations and symptoms that were part of the Total Illness Burden Index.[21] The Total Illness Burden Index includes measures of 15 different disease categories and has been shown to be significantly associated with measures of functional status as well as with disability days and the use of health services.[21] We restricted our assessment of comorbidity to the three disease categories that assess cardiopulmonary disease, because these categories reflect the conditions that are most likely to influence the choice of primary tumor therapy and because we wanted to minimize respondent burden. In the resultant comorbidity measure, a positive score reflects above-average comorbidity.

We assessed physical function using the 10-item physical function subscale of the 36-item short form Medical Outcomes Study functional status questionnaire (SF-36), which is scaled from 0 to 100, with a higher score indicating better function. The SF-36 measures eight health concepts, including physical function, and was developed to represent well-validated, full-length parent scales without loss of statistical precision. Results from the Medical Outcomes Study indicate that the physical function subscale is reliable and clinically valid.[22]

Third, we considered tumor characteristics: tumor size (≤1 cm, >1–2 cm, >2 cm), estrogen receptor status (positive/negative), and lymph node status (positive/negative). Fourth, we considered patient-physician interactions associated with treatment decision-making: patients' perceptions of doctor-patient communication (a four-item measure that rates the quality of information about breast carcinoma given to patients by their physicians, as well as a physician's ability to give information, discuss treatment options, and tailor treatments to patient needs [Cronbach's $\alpha = 0.92$]), patients' ratings of their physicians' technical and interpersonal care (a four-item measure that rates physicians' personal manner, communication skills, technical skills, and overall care [Cronbach's $\alpha = 0.95$]), and patients' perceptions of their own ability to communicate with their physicians (a three-item measure that assesses patients' ability to give and receive information [Cronbach's $\alpha = 0.96$]). We also asked women about the number of times that breast carcinoma specialists discussed treatment options with them. This latter variable was the sum of affirmative responses to the question, "Did _____ discuss options for your breast carcinoma treatment with you?" This question was asked in relation to up to four breast carcinoma specialists with whom the patient had consulted, including surgeons (also second opinions), medical oncologists, and radiation oncologists. Affirmative responses were 78% for radiation oncologists, 83% for surgeons who performed the diagnostic biopsy (98% for second opinion surgeons), and 87% for medical oncologists. Finally, we asked whether family members were involved in the treatment decision-making process.

Analytic Strategy

Descriptive statistics were obtained for all study variables. We then performed a series of bivariate analyses, examining the relationships between each independent variable and the dependent variable, using two independent sample Student's t tests and chi-square tests as appropriate. Our bivariate analyses were performed using a three-level form of the dependent variable (radical mastectomy vs. breast-conserving surgery/axillary dissection/radiation therapy vs. all other therapies) to appreciate better the differences across these categories of primary tumor therapy.

In our multiple logistic regression analysis, we used a two-level form of the variable (definitive primary tumor therapy vs. all others) for four major reasons: 1) the majority of our subjects underwent breast-conserving surgery with axillary dissection followed by

radiation therapy; 2) modified radical mastectomy and breast-conserving surgery with axillary dissection followed by radiation therapy have been demonstrated to be equivalent with respect to mortality;[23] 3) as noted above, recent data suggest that older women who receive less-than-definitive treatment are more likely to die of their breast carcinoma than older women who receive definitive treatment;[3] and 4) logistic regression models with more than a two-level dependent variable are often difficult to interpret.

We took a conservative approach to developing our logistic regression model. Because of the importance of comorbidity, functional status, tumor size, and lymph node status in clinical decision-making, we forced these variables into our model. We then used stepwise multiple logistic regression techniques, with a significance criterion of 0.05 for entry or removal from the model for all other variables identified as being statistically significant on bivariate analysis.

Finally, in an effort to understand the results of our logistic regression analysis, we also performed a series of exploratory bivariate analyses, relating patients' ages and marital status to factors identified by the patients as being important in their decision-making about their breast carcinoma treatment.

RESULTS

Study Sample

Three hundred eighty-eight eligible patients were identified whose surgeons gave permission for contact. Of these, 302 (78%) agreed to participate. Patients who did not participate declined (n = 40), could not be contacted (n = 25), were in ill health (n = 13), or were non-English-speaking without a translator available (n = 8). Nonparticipants were an average of 3 years older than participants (71.2 vs. 68.4 years, $P = 0.01$). Equal proportions of participants and nonparticipants had Stage I (78%) and Stage II (22%) disease, respectively. No other information about nonparticipants was available.

Patient characteristics are displayed in Table 1. A little over half of our subjects were age ≥65 years (range, 55–97 years), and most were white. Half were married; most of the remainder were widowed. The majority had a high school education or greater. Their average comorbidity score was 7.06 (range, 3–20). The majority of patients had infiltrating ductal carcinoma and had Stage I disease. Stage I patients tended to be slightly older than Stage II patients (mean age, 68.9 vs. 66.6 years). In addition, older patients were more likely to be estrogen receptor positive (72% of patients age 55–64 years, 74% of those age 65–74 years, and 86% of those age 75+ years).

TABLE 1
Patient Demographics and Clinical Characteristics (n = 302)[a]

Characteristic	No. of patients (%)
Demographics	
Age (yrs)	
55–64	123 (41)
65–74	111 (37)
75+	65 (22)
Race	
White	280 (94)
African American	13 (4)
Other	7 (2)
Marital status	
Married	148 (49)
Widowed	98 (33)
Single	23 (8)
Divorced/separated	30 (10)
Education	
<High school	51 (17)
High school graduate	107 (36)
>High school	141 (47)
Health status	
Comorbidity (mean ± SD)	7.06 ± 2.4
Physical function (mean ± SD)	73.75 ± 21.61
Tumor characteristics	
Histology	
Infiltrating ductal	259 (86)
Infiltrating lobular	31 (10)
Other	12 (4)
Tumor size	
≤1 cm	85 (31)
>1–2 cm	128 (46)
>2 cm	65 (23)
Lymph node status	
Negative	241 (80)
Positive	60 (20)
Estrogen receptor status	
Positive	209 (76)
Negative	67 (24)
Primary tumor therapy	
Breast-conserving surgery/axillary dissection/ radiation therapy	169 (56)
Modified radical mastectomy	65 (21)
Other	
Breast-conserving surgery/radiation	26 (9)
Breast-conserving surgery/axillary dissection	22 (7)
Breast-conserving surgery alone	10 (3)
Miscellaneous	10 (3)

SD: standard deviation.
[a] Because values are missing, not all categories add up to 302.

Treatment Priorities

We asked our subjects about factors that were important in their decision-making. Two factors were rated very important by almost all patients (100% and 96%, respectively): 1) minimizing the possibility of recurrence, and 2) their doctors' recommendations. Although there was less consensus, also very important

to the majority were quality of life after treatment (77%) and their family's opinion (52%). A substantial minority also rated as very important what they would have to pay over and above what their insurance would cover and problems they would experience after surgery (28% and 22%, respectively). In contrast, 3 treatment-related factors were rated as *not* important at all by the majority of patients: 1) effects of treatment on sexuality (83%), 2) difficulty getting to and from treatments (65%), and 3) effects of treatment on looks (63%).

Predictors of Definitive Primary Tumor Therapy

In contrast to patterns of care observed elsewhere among older women with breast carcinoma,[8,10–12] the majority of women in our study underwent breast-conserving surgery and axillary dissection followed by radiation therapy (Table 1). Less than a quarter received a modified radical mastectomy. The remaining quarter received 1) breast-conserving surgery and radiation therapy, but no axillary dissection (n = 26); 2) breast-conserving surgery and axillary dissection, but no radiation therapy (n = 22); 3) breast-conserving surgery alone (n = 10); or 4) other (n = 10), such as radiation therapy only, incisional biopsy only, or simple mastectomy with or without radiation therapy.

The bivariate relationships between each of the independent variables and primary tumor therapy, categorized as modified radical mastectomy, breast-conserving surgery with axillary dissection followed by radiation therapy, or other therapies, are displayed in Table 2. Age, marital status, education, physical function, tumor size, lymph node status, and the number of times breast carcinoma specialists discussed treatment options were each significantly associated with the type of primary tumor therapy received ($P < 0.05$).

To understand the independent contributions of variables identified as statistically significant on bivariate analysis, we developed a multiple logistic regression model (Table 3) that controlled for comorbidity, physical function, tumor size, and lymph node status. Patient age, marital status, and the number of times breast carcinoma specialists discussed treatment options were independently and significantly associated with the receipt of definitive primary tumor therapy (modified radical mastectomy or the combination of breast-conserving surgery, axillary dissection, and radiation therapy). Older women, women who were not married, and women with whom treatment options were discussed less frequently were *less likely* to receive definitive primary tumor therapy, after taking into account differences in health status and tumor characteristics.

In an attempt to understand whether patient preferences were the reasons why age and marital status remained significant predictors of primary tumor therapy after statistical control for such potentially important confounders as comorbidity, physical function, tumor size, and lymph node status, we performed a series of bivariate analyses, relating patients' ages and marital status to factors identified by them as being important in their decision-making about their breast carcinoma treatment. With respect to age, the only issue of importance that differed by age was whether women had other responsibilities, such as caring for other family members. About 20% of women among those ages 55–64 years and among those ages 65–74 years indicated that this was a very important consideration, whereas only 7% of the group age 75+ years indicated that it was very important ($P < 0.01$). In fact, 83% of the group age 75+ years indicated that this consideration was not important at all.

Three factors related to marital status emerged as being important in women's treatment decision-making. Women who were not married were more likely to indicate that the problems they would experience after surgery ($P < 0.05$) and what they would have to pay over and above what their insurance would cover ($P < 0.01$) were very important considerations in their treatment decision-making. In contrast, married women, as with younger women, reported that having other responsibilities was a very important consideration ($P < 0.01$).

DISCUSSION

In this study of age-related variations in the treatment of patients with early stage breast carcinoma in the 1990s, we found that the majority (56%) of women underwent breast-conserving surgery and axillary dissection followed by radiation therapy. This percentage is higher than that observed even among younger women[10,12] and is in keeping with the fact that the Northeast has among the highest rates of breast-conserving surgery in the United States, even among older women.[24,25] In addition, age, marital status, and an indicator of patient-physician interactions (the extent to which breast carcinoma specialists discussed treatment options) were all independently associated with the receipt of definitive primary tumor therapy by older women with early stage breast carcinoma. These associations persisted after statistical control for comorbidity, physical function, and relevant tumor characteristics.

The inability of these latter factors to explain completely the age-related treatment variations in breast carcinoma care is in agreement with the findings of other investigators but requires explanation.[6,8,11,26] It is possible, for example, that we inadequately con-

TABLE 2
Factors Associated with Primary Tumor Therapy (n = 302)

Factors	No. of patients (%)		
	Modified radical mastectomy	Breast-conserving surgery/AD/RT	Other therapies
Demographics			
Age[a]			
55–64	34 (28)	77 (62)	12 (10)
64–74	20 (18)	73 (66)	18 (16)
75+	11 (17)	17 (26)	37 (57)
Marital status[a]			
Married	37 (25)	93 (63)	18 (12)
Not married	28 (19)	75 (49)	49 (32)
Education[a]			
<High school	8 (16)	22 (43)	21 (41)
≥High school	57 (23)	146 (59)	45 (18)
Health status (mean score)			
Comorbidity	6.91	7.03	7.27
Physical function[a]	72.46	76.69	67.22
Tumor characteristics			
Tumor size[a]			
≤1 cm	8 (9)	53 (62)	24 (28)
>1–2 cm	16 (12)	79 (62)	33 (26)
>2 cm	29 (45)	29 (45)	7 (10)
Estrogen receptor status			
Positive	42 (20)	122 (58)	45 (22)
Negative	19 (28)	37 (55)	11 (17)
Lymph node status[a]			
Negative	43 (18)	134 (56)	64 (26)
Positive	22 (37)	35 (58)	3 (5)
Patient-physician interaction (mean score)			
Doctor-patient communication	93.17	92.05	92.19
Technical and interpersonal care	95.29	94.90	96.15
Perceptions of abilities to communicate	71.28	71.90	67.76
No. of times treatment options were discussed[a]	2.6	2.23	2.1
Family member participation in treatment decision-making			
Yes	21 (23)	57 (64)	12 (13)
No	44 (21)	112 (55)	50 (24)

AD: axillary dissection; RT: radiation therapy.
[a] $P < 0.05$.

trolled for variations in health status and tumor prognostic factors in our multiple logistic regression model. We relied on women's reports of cardiopulmonary diseases and symptoms for our measure of comorbidity and on their reports of the physical limitations that were due to their health. However, recent studies from Europe have documented that older patients can accurately report whether or not they have cardiovascular disease,[27,28] and our measure of physical function has been used widely in studies of older persons and has been shown to be sensitive to low levels of morbidity.[29,30] Furthermore, in our study, older women reported more comorbidity and poorer physical function than younger women, as would be expected (Table 1). Finally, we performed an additional multiple logistic regression analysis, excluding women age 75+ years with very small tumors (<1 cm). In this analysis, age persisted as an independent predictor of definitive primary tumor therapy.

We believe that clinical uncertainty as to the most appropriate therapies for older women affords the best explanation for the age-related variations that we have observed. In particular, there is controversy about the necessity of axillary dissection as well as that of radiation therapy following breast-conserving surgery for older women. Questions about axillary dissection relate to its diagnostic versus therapeutic value;[31] questions about postoperative radiation therapy arise because it has not been demonstrated to affect survival rates and also because it may not be necessary for

TABLE 3
Multiple Logistic Regression Model Predicting Receipt of Definitive Primary Tumor Therapy[a]

Variable	β-coefficient	Odds ratio (95% CI)
Tumor size		
≤1 cm (referent)	—	—
>1–2	0.2948	1.34 (0.62, 2.89)
>2	1.5372	4.65 (1.48, 14.65)
Lymph node status (positive/negative)	1.3265	3.77 (1.02, 13.95)
Age group		
55–64 yrs	2.3032	10.01 (3.78, 26.47)
65–74 yrs	1.8580	6.41 (2.68, 15.35)
75+ yrs (referent)	—	—
Marital status (married/not married)	0.8961	2.45 (1.17, 5.15)
No. of times treatment options were discussed (continuous)	0.5423	1.72 (1.14, 2.61)

CI: confidence interval.
[a] Adjusted for comorbidity and physical function.

achieving acceptably low recurrence rates in older women.[32–34] It is clear from our data and those of others that axillary dissection and radiation therapy are being used preferentially less often in older women than in younger women. Among our patients, adjuvant systemic therapy (usually tamoxifen) appears to have been substituted for these procedures in about two-thirds of women who did not receive standard primary therapy. Whether this substitution results in similar outcomes is not known definitively, although there is case-series evidence suggesting that this strategy may be appropriate for older women with T1 tumors.[35,36]

Our findings confirm and extend the work of previous investigators who have found that being unmarried is a risk factor for not receiving definitive therapy for breast carcinoma.[10,13]

The older unmarried women in our study were more concerned than married women about treatment-related problems that they might experience after surgery and the out-of-pocket costs of their care. Both of these concerns may have led them to choose less intense primary tumor therapy regimens. Whether their surgeons tended to offer such regimens preferentially to them is not known.

In this regard, an important finding in our study was the influence of the extent to which treatment options were discussed regarding the primary tumor therapies received by older women. Others have found that older women are less likely to receive medical or radiation oncologist consultations[7,37] and that being offered a choice is more strongly related to psychosocial outcomes than is the type of treatment.[38] We believe that if patients are offered choices and are encouraged to be involved in their care, the decisions that they and their physicians make may more closely reflect their own values and preferences. When they are not, the decisions made may more closely reflect the values and beliefs of their physicians. Here, clinical uncertainty (or biases) about what represents appropriate care may have an important influence on physician-directed decisions.

Our findings are provocative, but they must be interpreted with the following limitations in mind. First, we studied the care of women who were mainly white, well-educated, and older in clinical settings with academic affiliations in one geographic region (Boston, Massachusetts). Second, selection factors resulted in our studying younger members, on average, of the eligible patient population. However, we believe that studies of older and more diverse patient populations may find an even larger impact of age, marital status, and patient-physician interactions on outcomes than we did. Third, we relied on women's recall of events and treatment decision-making that had occurred several months previously. Details of physician visits and thought processes may have been forgotten or recalled imperfectly. It seems unlikely, however, that this should have occurred differentially across treatment groups. Finally, our measure of the extent to which treatment options were discussed was based on counts of reported discussions rather than an actual measure of the depth and extent of discussions, such as would be available from audio or videotaping or from direct observation.

With these limitations in mind, it is clear that additional studies are needed that focus on both the process and the outcomes of care for older women with breast carcinoma. Such studies must take into account comorbidity, functional status, and tumor characteristics, and must link therapies received with the important clinical outcomes of functional status, breast carcinoma recurrence, and breast carcinoma specific mortality. Such studies are particularly important because the most recent breast carcinoma mortality figures demonstrate a marked decline in mortality in all age groups except those age 80 years or older. Furthermore, the mortality rate in those ages 70–79 years did not decline between 1991 and 1993, as it did in every younger age group.[39]

It is noteworthy that almost all of the women in this study reported that minimizing the possibility of recurrence their doctors' recommendations were both very important considerations in their treatment decision-making. Our older patients may therefore be better served if we recommend definitive therapies or recommend that they participate in clinical trials and/or observational studies designed to answer the critical questions of treatment efficacy and effectiveness in

older persons. In discussing therapies with them, we must be sensitive to their fears and concerns about the monetary costs and functional consequences of treatment in relation to the expected benefits.

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Breast Cancer Care in Older Women

Sources of Information, Social Support, and Emotional Health Outcomes

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BACKGROUND. The authors studied older women with breast cancer and asked: 1) where do older women get information regarding breast cancer care and how helpful do they perceive each of these sources to be? and 2) what aspects of social support are associated with older women's general and breast cancer specific emotional health outcomes?

METHODS. To be eligible, women had to be at least 55 years of age and newly diagnosed with TNM Stage I or II breast cancer. Data were collected from women's surgical records and a 35-minute, computer-assisted telephone interview.

RESULTS. Nearly all women rated information that was provided by their breast cancer physicians as very or somewhat helpful. Written materials provided by breast cancer physicians also were frequently rated as very or somewhat helpful. Women's marital status, religious service attendance, ratings of their physicians' technical and interpersonal care, and perceptions of their own abilities to communicate with their physicians were significantly associated with both general and breast cancer specific emotional health outcomes (all $P < 0.05$).

CONCLUSIONS. Although older women obtained information regarding breast cancer from a variety of sources, they relied heavily on their physicians for information. To care most effectively for this group of patients, an increased understanding of the relation between the processes and outcomes of breast cancer care is needed Identifying older women with breast cancer at risk for poor emotional health outcomes and developing methods to enhance physician-patient communication in this setting may improve these outcomes. ***Cancer* 1998;83:706–11.**
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KEYWORDS: older women, breast cancer, emotional health, physician-patient communication.

Sixty percent of incident cases of breast cancer are diagnosed in women age ≥ 60 years.[1] This percentage is likely to grow, not only because older age is the most important risk factor for breast cancer, but because of gains in life expectancy and decreases in deaths due to cardiovascular disease. To most effectively care for this growing group of women, we need to understand the relation between the processes and outcomes of breast cancer care.

Over the past decade, investigators who have focused on age-related variations in breast cancer care have documented that older women are at greater risk for receiving less than definitive treatment.[2–10] We recently reported that, in addition to older age, being unmarried and having treatment options discussed less frequently also are risk factors for the receipt of less than definitive primary tumor therapy.[10] Newer studies suggest that the receipt of less than definitive care is associated with both higher recurrence rates and higher mortality rates among older women.[11,12]

In contrast, comparatively less attention has been paid to the relation between processes of care and quality-of-life outcomes among older women. As the proportion of older women who are longer term survivors of breast cancer continues to grow, this relation will assume greater importance, particularly if it is demonstrated that variations in the process of care are related to variations in these quality-of-life outcomes. Although older women are in general at lower risk for adverse psychosocial outcomes than are their younger counterparts,[13–15] there are reasons to believe that some older women may be at higher risk because of inadequate social support, including poor communication between them and their physicians. First, older women frequently are single; 36% of women ages 65–74 years, 62% of women ages 75–84 years, and 80% of women age ≥ 85 years are widowed. In addition, the majority of women age ≥ 75 years live alone.[16] Second, although religious involvement appears to have a protective effect among older women with respect to depression, the converse also is true: older women with less religious involvement are at greater risk of depression.[17] Third, physicians tend to spend less time with their older patients than they spend with their younger patients.[18,19] In addition, they tend to be more egalitarian and provide better information, questioning, and support to their younger patients than to their older patients.[20] A recent study of older and younger breast cancer patients has documented similar findings.[21] And in studies of patients with various chronic diseases, a more participatory decision-making style of care on the part of their physicians (e.g., presenting options, discussing the pros and cons of these options, and eliciting patient preferences) has been associated with better functional and physiologic outcomes.[22]

With these considerations in mind, we studied older women with early stage breast cancer and asked the following questions: 1) where do older women receive information regarding breast cancer care and how helpful do they perceive each of these sources to be? and 2) what aspects of social support are associated with older women's general and breast cancer specific emotional health outcomes?

METHODS

Study Sample

The study's methods have been described elsewhere.[10] To be eligible for the study, women had to be age ≥ 55 years, newly diagnosed with TNM Stage I or II breast cancer, and have no previous history of breast cancer. Eligible women were sent an introductory letter and a consent form 2–3 months after their definitive surgical treatment. Our interviewer conducted follow-up by telephone, providing additional information regarding the study, answering questions, and obtaining informed consent.

Data Collection

Data were collected from women's surgical records and a 35-minute, computer-assisted telephone interview with consenting women. Data collected from medical records included: histology, stage, and surgeries performed (modified radical mastectomy or breast-conserving surgery). The patient telephone interview, conducted an average of 4.5 months after definitive surgical therapy, included questions regarding sociodemographic characteristics (including age, education, martial status, and religious service attendance); general health-related quality of life (as measured by the Medical Outcomes Study Short Form [SF-36][23]); breast cancer specific quality of life (with response options ranging from excellent [1] to poor [5]); the presence of physician-diagnosed cardiopulmonary diseases and the frequency of associated symptoms; the perceived helpfulness of various sources of information regarding breast cancer and its treatment (with response options ranging from very helpful [1] to not applicable, did not get information from this source [5]); the kinds of help that they did not have, but wished that they had to assist them with treatment decision-making; and ratings of their breast cancer specialists' technical and interpersonal care (with response options ranging from excellent [1] to poor [5]).

Major Analytic Variables

Outcome Variables

We considered two dependent variables in our analyses: 1) general emotional health, a 5-item measure of emotional health from the Medical Outcomes Study SF-36[23] that is scaled from 0–100, with a higher score indicating better emotional health (Cronbach's α = 0.83), and 2) breast cancer specific emotional health, a 4-item measure of feelings and worries due to potential problems associated with the progression of breast cancer, again scaled from 0–100, with a higher score indicating better breast cancer specific emotional health (Cronbach's α = 0.78). The four breast cancer specific items were: *Now that much of your treatment is behind you, how well do you feel you are doing with each of the following: 1) Dealing with feelings such as anger, fear, grief, and anxiety; 2) Worries about your family's ability to manage if you get sicker; 3) Worries about who will take care of you if you get sicker; and 4) Worries about recurrence of the cancer.*

Independent Variables

We considered indicators of social support from two categories: 1) women's informal social support: marital status (married/not married) and attendance at religious services (approximately once a week or more/lesser amounts); and 2) physician-patient communication associated with treatment decision-making: patients' perceptions of physician communication (a 4-item measure based on ratings of the quality of breast cancer information given to patients by their physicians, as well as physicians' abilities to give information, discuss treatment options, and tailor treatments to patient needs [Cronbach's $\alpha = 0.92$]); patients' ratings of their physicians' technical and interpersonal care (a 4-item measure based on ratings of physicians' personal manner, communication skills, technical skills, and overall care [Cronbach's $\alpha = 0.95$]); and patients' perceptions of their own abilities to communicate with their physicians (a 3-item measure based on patients' ratings of their abilities to get information from, and to give information to their physicians [Cronbach's $\alpha = 0.96$]). All physician-patient communication variables were scaled from 0–100, with higher scores indicating better ratings.

Covariates

We considered age, two measures of health status (comorbidity and perceptions of change in health status), and type of surgery as covariates. We divided age into three categories: 55–64 years, 65–74 years, and 75+ years. We assessed comorbidity using a continuous measure that ranged in score from 3–20 and was based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease and related disease manifestations and symptoms that were part of the Total Illness Burden Index.[24] We also included women's perceptions of change in their health status during the previous year (an item from the SF-36).[23] This measure was scaled from 0–100 with a higher score indicating better health status. Type of surgery was classified as modified radical mastectomy versus breast-conserving surgery.

Analytic Strategy

We first obtained descriptive statistics on all study variables, which allowed us to address our first study question regarding the sources of information about breast cancer accessed by women and their perceived helpfulness. We also assessed the relation between each source of information and women's age, education, and marital status using chi-square tests. We then identified factors associated with patients' general and breast cancer specific emotional health outcomes. In the first phase of the analysis we investigated the distributional properties of our two dependent variables and our array of independent variables. Next, we examined bivariate relations between the independent variables and each dependent variable using two independent sample Student's t tests and correlation analysis. We selected independent variables for potential inclusion in regression models based on significance with each dependent variable ($P < 0.05$). Once a pool of candidate-independent variables was identified, bivariate relations between the independent variables were examined to assess multicolinearity. In the final stage of the analysis we developed multiple linear regression models relating the two dependent variables, considered separately, to selected independent variables.

RESULTS

Study Sample

Three hundred eighty-eight eligible women were identified, 302 of whom (78%) agreed to participate. They ranged in age from 55–97 years. Nearly half were married (49%) and nearly one-third (34%) attended religious services once or more per week. Mean scores on health status indicators were as follows: comorbidity = 7.06 (range, 3–20); health transitions = 44.95 (range, 0–100); general emotional health = 74.01 (range, 12.5–100); and breast cancer specific emotional health = 65.95 (range, 6.25–100). Twenty-one percent of these women underwent modified radical mastectomy.

Perceived Helpfulness of Sources of Information Regarding Breast Cancer

When asked about the helpfulness of breast cancer-related information received from a variety of sources, the information that was provided by their breast cancer physicians was rated as very or somewhat helpful by nearly all women (Table 1). Written materials provided by breast cancer physicians also were frequently rated as very or somewhat helpful. Of less perceived helpfulness was written information obtained from sources other than their breast cancer physicians, and information provided by friends and family, by television specials, and by primary care physicians. Note that substantial numbers of women did not access information from these latter four sources. When we restricted the analysis to only those who actually obtained information from a given source, all ratings improved. However, their rank ordering changed very little, with the exception that television specials were rated slightly lower than primary care physicians (see Table 1, percentages in brackets).

TABLE 1
Sources of Information Regarding Breast Cancer (n = 302)

Source	Perceived helpfulness: Very or somewhat helpful No. (%) [%][a]	Perceived helpfulness: Not very or not helpful at all No. (%)	Not applicable (did not get information from this source) No. (%)
Breast cancer physicians or staff	294 (99)[99]	2 (1)	0
Written materials from breast cancer physician	248 (84)[95]	12 (4)	36 (12)
Other written materials obtained by patient	198 (67)[92]	17 (6)	81 (27)
Friends and family	161 (54)[84]	30 (10)	105 (36)
Television specials	139 (47)[68]	65 (22)	92 (31)
Primary care physician	120 (41)[72]	46 (15)	130 (44)

[a] Second percentage shown is a recalculation of the percentage that excludes the responses from the category "Not Applicable."

We also examined the relation between age, education, and marital status and women's ratings. The oldest women (age 75+ years) were most likely not to have obtained written information from sources other than their breast cancer physicians (43% vs. 33% of those ages 65–74 years, and 15% of those ages 55–64 years; $P = 0.001$) or from friends and family (50% vs. 38% of those ages 65–74 years, and 27% of those ages 55–64 years; $P = 0.04$). When we restricted the analysis to those who actually obtained information from these sources, the youngest group of women (ages 55–64 years) were more likely to have found the written information that they had obtained to be very or somewhat helpful (98% vs. 89% of those ages 65–74 years, and 79% of those age 75+ years; $P = 0.001$); there was no difference by age with respect to the perceived helpfulness of information from friends and family. Educational attainment and marital status were not related to whether information was obtained from a particular source, nor its perceived helpfulness.

When asked about the kinds of help with treatment decision-making that they did not have but wished that they had, 60% of women wished that they had someone with them at appointments when treatment options were discussed; 39% wished that they had help with knowing what questions to ask.

TABLE 2
Results of Multiple Regression Analysis: General Emotional Health[a]

Independent variable	Standardized parameter estimate	*P* value
Marital status	0.1495	0.008
Religious service attendance	0.1418	0.011
Physician's interpersonal and technical care	0.1381	0.016
Patient's ability to communicate with her physician	0.1184	0.04

[a] Adjusted for comorbidity and change in health status.
R square = 0.16.

TABLE 3
Results of Multiple Regression Analysis: Breast Cancer Specific Emotional Health[a]

Independent variable	Standardized parameter estimate	*P* value
Marital status	0.1865	0.0009
Religious service attendance	0.1124	0.042
Physician's interpersonal and technical care	0.1594	0.006
Patient's ability to communicate with her physician	0.1636	0.005

[a] Adjusted for comorbidity and change in health status.
R square = 0.16.

Women's General and Breast Cancer Specific Emotional Health

To determine whether women's informal social support and aspects of physician-patient interactions were related to their general and breast cancer specific emotional health, we developed separate multiple regression models. We included age and type of surgery as independent variables in the models but they did not add statistically or substantively, and therefore were removed from the models.

With general emotional health as the dependent variable and controlling for comorbidity and change in health status in the previous year, women's marital status, their religious service attendance, their ratings of physicians' technical and interpersonal care styles, and their perceptions of their own abilities to communicate with their physicians were statistically significant (Table 2). Similarly, with breast cancer specific emotional health as the dependent variable and controlling for comorbidity and change in health status, the same four variables also were statistically signifi-

cant (Table 3). With the exception of regular religious service attendance, the relations between the independent variables and breast cancer specific emotional health were stronger than those between independent variables and general emotional health.

DISCUSSION

Consistent with the published literature,[25] we found that older women value highly the information provided by their breast cancer physicians. In addition, the women that we studied, particularly the youngest women (those ages 55–64 years), accessed other sources of information that most considered to be of value, presumably because these sources complemented and reinforced information provided by their physicians.[26] Of concern, these women perceived their primary care physicians to be one of the least helpful sources of information regarding breast cancer care. As our nation moves toward models of care that increasingly rely on primary care physicians, these front-line physicians will need to have access to up-to-date, high quality information regarding cancer care appropriate for different subsets of patients. Furthermore, if primary care physicians are to provide the majority of follow-up care for breast and other cancer survivors, they must understand treatment as well as follow-up care issues.[27] This information will be particularly important for older women, because these women are more likely to have a greater burden of comorbid illness and functional disability. They also are more likely to have long-standing relations with their primary care physicians than with their breast cancer physicians.

In addition, the circumstances surrounding breast cancer treatment decision-making appear to have been suboptimal for a substantial proportion of women. They indicated that they would have benefited from having someone with them at appointments when treatment options were discussed and from having help with knowing what questions to ask in relation to breast cancer and its treatment. In this regard, it is noteworthy that women's perceptions of their abilities to communicate with their physicians were statistically significantly associated with both general and breast cancer specific emotional health. Women who rated their abilities less highly had lower emotional health scores, even after controlling for health status and other social support indicators.

The setting of newly diagnosed breast cancer probably is not the best time to try to enhance patients' abilities to communicate with their physicians. Furthermore, it is not clear whether communication skills learned in the setting of chronic disease care can be translated to an acute crisis situation. Nonetheless, awareness of women's insecurities with their communication skills, in addition to the presence of other risk factors for adverse outcomes, may help target those women who might benefit most from the extra time and effort required to involve them to a greater extent in the treatment decision-making process. Our regression models suggest that these other risk factors may include being unmarried and not being an active participant in a religious community. Indeed, the associations that we found between marital status and religious service attendance and our emotional health measures are consistent with previous literature documenting the benefits of social support[28] and add to the growing body of literature documenting the positive relation between religious service attendance and health outcomes.[29]

The additional positive association between patients' ratings of their physicians' technical and interpersonal care and our two measures of emotional health further emphasize the critical importance of physician-patient communication in the management of breast cancer in older women. As noted earlier and as documented by others, older patients frequently rely on their physicians to make treatment decisions for them.[30] Physicians may need to work harder to involve their older patients in care decisions than their younger patients, particularly those who have additional insecurities regarding their own communication skills and those who lack social support. The challenges associated with this effort are considerable, especially given current pressures to decrease rather than increase the amount of time physicians spend with patients.[31] However, the benefits are likely not only to improve decision-making with respect to treatment,[10] but with regard to better emotional health outcomes as well.[15]

Our study has several limitations that must be taken into account when interpreting its findings. First, we studied largely white, well educated older women in clinical settings with academic affiliations in one geographic region. Second, differential response rates resulted in our studying younger members, on average, of the eligible patient population. Both factors limit our ability to generalize our results. However, in this regard it is difficult to know whether the observed relations might have been stronger or weaker had we been able to study a more heterogeneous sample.

Third, our data are cross-sectional and therefore preclude definitive statements regarding cause and effect. Fourth, we relied on self-reported recalled information because we were neither able to observe directly physician-patient encounters nor to audiotape or videotape them. Nonetheless, we believe that

our findings support several conclusions. Although women obtain information regarding breast cancer from a variety of sources, they rely heavily on their physicians for information on breast cancer and its treatment. Given clinical uncertainty as to what represents the most appropriate therapy for older women, we believe that it is all the more important that physicians offer them choices so that their decisions reflect their values and preferences.[10] In addition, identifying older women with breast cancer at risk for poor emotional health outcomes and developing methods to enhance physician-patient communication in this setting may improve these outcomes.

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Report

Risk factors for a decline in upper body function following treatment for early stage breast cancer

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Key words: breast cancer treatment, older women, upper body function

Summary

Purpose: To identify risk factors for a decline in upper body function following treatment for early stage breast cancer.

Methods: We conducted a cross-sectional observational study of 213 women ≥ 55 years of age newly diagnosed with early stage breast cancer interviewed three to five months following their definitive surgery. Patients were classified as having impaired upper body function related to their breast cancer treatment if: 1) they reported having no difficulty in performing any of three tasks requiring upper body function (pushing or pulling large objects; lifting objects weighing more than 10 pounds; and reaching or extending arms above shoulder level) prior to treatment, but reported that any of these tasks were somewhat or very difficult in the four weeks prior to interview, or 2) they reported that performing any of the three tasks requiring upper body function was somewhat difficult prior to treatment, but reported that any of these tasks were very difficult in the four weeks prior to interview.

Results: In multiple logistic regression models, both the extent and type of primary tumor therapy and cardiopulmonary comorbidity were significantly associated with a decline in upper body function following breast cancer treatment.

Conclusion: Given the critical importance of upper body function in maintaining independent living, clinicians should consider the functional consequences of treatment when they discuss treatment options and post-operative care with older women who have early stage breast cancer.

Introduction

Breast cancer has become increasingly common among older women. The incidence of breast cancer increases with age until at least the ninth decade of life, the number of older women at risk has increased, and the age-adjusted incidence has increased, in part due to increased use of screening mammography [1]. Furthermore, the increasing use of screening mammography has resulted in a greater proportion of older women being diagnosed with early stage disease [2]. Earlier diagnosis, coupled with an overall increase in longevity in late life, will likely result in an increase in the number of older women who are long-term survivors of breast cancer. For these women, the functional consequences of breast cancer treatment, manifested in tasks that require upper body strength, are likely to assume greater importance, particularly as they concomitantly acquire age-related disabilities.

Satariano and colleagues studied the functional consequences of breast cancer therapy and found that among women aged 55–74 who were treated for breast cancer, at three months following diagnosis they were more likely than controls without breast cancer to report difficulty in completing tasks that required upper body strength [3]. In another study by the same investigative team, analyses conducted with the case group failed to find a treatment effect. However, the treatment measure categorized radiation, chemotherapy, and hormonal therapy together as 'adjuvant therapy'. Thus, it was not possible to evaluate the effects of standard therapies or of the

specific components of these therapies on upper body function [4].

Because tasks that require upper body strength are crucial for maintaining independence, it is important to identify risk factors for breast cancer patients' decline in abilities to perform such tasks. Knowledge of these risk factors may aid in the identification of women at high risk for poor functional outcomes and in the choice of their primary breast cancer treatment.

We therefore conducted a cross-sectional study of women $\geq$ 55 years of age at three to five months after their treatment for newly diagnosed stage I and stage II breast cancer to identify risk factors for a decline in upper body functional abilities in relation to treatments received.

Methods

Sampling

Details of the study have been descibed elsewhere [5]. In brief, we studied women $\geq$ 55 years of age, newly diagnosed with histologically confirmed stage I and stage II invasive breast carcinoma cared for at one of five hospitals in Boston, Massachusetts. Potential study participants were sent an introductory letter signed by their surgeon and a consent form at approximately two to three months following their definitive surgical treatment. An interviewer followed-up with a telephone call to explain the study further, to answer questions, and to obtain informed consent. We restricted the analyses described herein to those women interviewed three to five months following their definitive surgery to minimize variation associated with differing length of recovery time.

Data collection

Data were collected via a review of patients' surgical records and a 35 min computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included: tumor size, axillary node status, breast surgery or surgeries performed (mastectomy or breast conserving surgery, with or without axillary dissection), and whether or not the patient received a course of post-operative radiation therapy. The patient telephone interview included questions about tasks that required upper body function and were asked in relation to breast cancer treatment:

1. pushing or pulling large objects, such as a living room chair,
2. lifting objects weighing more than 10 pounds, such as a heavy bag of groceries, and
3. reaching or extending arms above shoulder level.

For each task, the subject was asked about its difficulty (very, somewhat, or not difficult) in performance during four weeks preceding interview as well as prior to their breast cancer treatment. These items were selected from the items used by Satariano and colleagues [3], fielded previously in the Framingham Disability Study [6] and derived from the original work of Nagi [7]. In addition, we asked questions about cardiopulmonary comorbidities that were part of the Total Illness Burden Index [8], as well as about demographic characteristics (age, race, marital status, education, height, and weight).

Major analytic variables

Our dependent variable was a decline in upper body function in relation to breast cancer treatment. Patients were classified as having a decline in upper body function in relation to their breast cancer treatment if:

1. they reported having no difficulty in performing any of the three tasks requiring upper body function prior to treatment, but reported that any of these tasks were somewhat or very difficult in the four weeks prior to interview, or
2. they reported that performing any of the three tasks requiring upper body function was somewhat difficult prior to treatment, but reported that any of these tasks were very difficult in the past four weeks.

For our independent variables we considered: age (55–64, 65–74, 75+ years) and education ($<$ high school/ $\geq$ high school). We also considered body mass index (BMI: weight in kilograms divided by height in meters squared); comorbidity (a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease and related symptoms, with a positive score reflecting above average comorbidity); breast cancer characteristics, including tumor size ($\leq$1 cm, $>$1–2 cm, $>$2 cm) and node status (positive/negative); and breast cancer treatments received. For the breast cancer treatments variables, we used two different approaches. First, we considered each of the two standard treatments (modified radical mastectomy and breast conserving surgery with axillary dissection followed by radiation therapy) in comparison to other primary therapies received (e.g. breast conserving surgery without radiation therapy). Second, we considered the specific components of primary tumor

therapy (axillary dissection, definitive surgery [mastectomy vs. breast conserving surgery], and radiation therapy).

Analytic strategy

We obtained descriptive statistics for all study variables. We then performed a series of bivariate analyses, examining the relationships between independent variables and the dependent variable, using independent samples t-tests and Chi-square tests as appropriate. Next, we developed multiple logistic regression models whose independent variables included all the statistically significant associations ($p < 0.05$) found in bivariate analyses, as well as all breast cancer treatment variables. We used stepwise multiple logistic regression techniques with significance criterion of 0.1 for entry or removal from the model.

Results

Two hundred thirteen women (71%) from the original cohort were interviewed three to five months following their definitive surgery and served as the study sample for this analysis. Sample characteristics are similar to those of the full cohort [5]. Almost two-thirds (59%) were $\geq$ 65 years of age. Most were white (95%) and had a high school education or greater (84%). Half were married; most of the remainder were widowed. The average BMI was 25.98 ($\pm$5.05) and the average comorbidity score was 1.48 (range 0–15). Most patients had small tumors (77% $\leq$ 2 cm) and were node negative (80%). The majority (57%) had undergone breast conserving surgery with axillary dissection followed by radiation therapy; 23% had undergone modified radical mastectomy. Of the 43 who received other than these standard primary tumor therapies, 23 underwent breast conserving surgery followed by radiation but without axillary dissection; 12 underwent breast conserving surgery and axillary dissection but did not receive radiation therapy; five underwent breast conserving surgery but neither axillary dissection nor radiation therapy; and the remainder either underwent simple mastectomy without radiation ($n = 2$) or underwent biopsy or radiation therapy only ($n = 2$). About a third of all subjects (35%) reported a decline in upper body function following their breast cancer treatment.

On bivariate analysis (Table 1), women who reported a decline in upper body function since breast cancer treatment had higher BMIs and cardiopulmonary comorbidity scores than those who did not report worsened upper body function. In addition, women who received other than standard primary tumor therapies were less likely to report worsened upper body function than those who received either breast conserving surgery with axillary dissection and radiation therapy or a modified radical mastectomy (23% vs. 36% and 42%, $p = 0.15$). With respect to the individual components of primary tumor therapy, women who underwent axillary dissection, mastectomy, or radiation therapy were all somewhat more likely to report a decline in upper body function since treatment than those who did not, but none of these relationships reached statistical significance.

In a multiple logistic regression model that included standard therapies (modified radical mastectomy and breast conserving surgery with axillary dissection followed by radiation therapy), with non-standard primary tumor therapies as the referent group (Table 2, Model 1), women who received breast conserving surgery with axillary dissection and follow-up radiation therapy were 2.2 times more likely to report a decline in upper body function ($p = 0.08$), and women who received modified radical mastectomy were 2.8 times more likely to experience a decline in upper body function ($p = 0.04$). Cardiopulmonary comorbidity was also an independent predictor of a decline in upper body function ($p = 0.002$). In a second multiple logistic regression model (Table 2, Model 2), women undergoing mastectomy or radiation therapy were each more than six times more likely to report a decline in upper body function than those who did not ($p = 0.01$). As in Model 1, cardiopulmonary comorbidity also was an independent predictor of a decline in upper body function following breast cancer treatment ($p = 0.006$).

Discussion

We have found that among older women with early stage breast cancer, the extent of primary tumor therapy, as well as specific components of therapy, and self-reported cardiopulmonary comorbidity are risk factors for a decline in upper body function during the early months following primary breast cancer therapy. To our knowledge, this is the first study to evaluate both the early effects of different treatment regimens as well as comorbidity in a group of older women with early stage breast cancer.

Sneeuw and colleagues examined late functional outcomes (an average of four years after treatment) among women of various ages who received breast conserving surgery, axillary dissection, and radiation therapy. In this study from the Netherlands of 76 women (age range 37–75) who were treated between

Table 1. Bivariate relationships between patient characteristics and decline in upper body function ($n = 213$)

Characteristic	Declined ($n = 74$)	Not declined ($n = 139$)	p Value
Demographic characteristics			
Age (n, %)			
55–64	30 (34)	58 (66)	0.97
65–74	30 (36)	54 (64)	
75+	14 (34)	27 (66)	
Education (n, %)			
< High school	14 (40)	21 (60)	0.50
≥ High school	60 (34)	116 (66)	
General health status (mean, SEM)			
Body mass index (BMI)	26.95 (0.67)	25.45 (0.40)	0.054
Comorbidity	2.27 (0.41)	1.07 (0.17)	0.009
Breast cancer characteristics			
Tumor size (n, %)			
≤1 cm	19 (32)	41 (68)	0.76
>1–2 cm	33 (36)	59 (64)	
>2 cm	18 (38)	29 (62)	
Node status (n, %)			
Negative	57 (34)	113 (66)	0.58
Positive	16 (38)	26 (62)	
Breast cancer treatments			
Primary tumor therapy (n, %)			
Modified radical mastectomy	22 (42)	31 (58)	0.15
Breast conserving surgery/ axillary dissection/radiation therapy	43 (36)	77 (64)	
Other	9 (23)	31 (77)	
Specific treatment modalities (n, %)			
Axillary dissection			
Yes	65 (36)	117 (64)	0.33
No	8 (27)	22 (73)	
Mastectomy			
Yes	22 (42)	31 (58)	0.23
No	52 (33)	108 (67)	
Radiation therapy			
Yes	54 (37)	93 (63)	0.36
No	20 (30)	46 (70)	

1975 and 1985, nearly half of the subjects reported a little (34%) or moderate (13%) limitation of movement in the arm and shoulder on the treatment side [9]. Gerber and colleagues compared functional outcomes among participants in a randomized clinical trial who received either modified radical mastectomy or breast conserving surgery with axillary dissection and follow-up radiation therapy. All subjects also participated in an extensive structured rehabilitation program. The average number of days to reach functional range of motion did not differ between the groups, but twice as many women who were treated in the breast conserving surgery treatment group reported chest wall tenderness one year after treatment, as compared to the women in the modified radical mastectomy treatment arm (58.4% vs. 27.4%, $p < 0.0001$) [10]. These data suggest that

Table 2. Multiple logistic regression models predicting a decline in upper body function in relation to breast cancer treatment

Characteristics	β coefficient	Odds ratio (95% CI)
Model 1		
Primary tumor therapy		
Other (referent)	–	–
Breast conserving surgery	0.7863	2.20 (0.92, 5.23)
Modified radical mastectomy	1.0322	2.81 (1.08, 7.32)
Cardiopulmonary comorbidity	0.1721	1.19 (1.06, 1.33)
Model 2		
Mastectomy	2.0377	7.67 (1.66, 35.55)
Radiation therapy	1.8826	6.57 (1.45, 29.87)
Cardiopulmonary comorbidity	0.1560	1.17 (1.05, 1.31)

breast conserving surgery in conjunction with axillary dissection and radiation therapy may have substantial late functional consequences.

Our data are consistent with these investigations and extend those of Satariano and colleagues [3, 4]. They demonstrate that there are early functional consequences among older women who receive either modified radical mastectomy or breast conserving surgery with axillary dissection followed by radiation therapy, although the risk associated with modified radical mastectomy is greater. Furthermore, our treatment component-specific analyses suggest that radiation therapy contributes to the increased risk of functional decline among women who undergo breast conserving surgery, in keeping with the findings of Gerber and colleagues [10]. In our data, axillary dissection does not appear to have an independent influence, once the effects of type of surgery and radiation are taken into account. This may be because our measure of upper body function was insensitive to the difficulties experienced by women who undergo axillary dissection, or because the number of women who did not receive axillary dissection was relatively small. The advent of lymphatic mapping and sentinal lymph node biospy may decrease substantially the need for axillary dissection in the not distant future [11].

Finally, cardiopulmonary comorbidity burden also is a risk factor for a decline in upper body function following primary tumor therapy. Tasks that require upper body strength stress the cardiopulmonary system. Thus, cardiopulmonary disease burden may limit rehabilitation efforts during the early treatment recovery period.

Of interest, the group of women at least risk for a decline in upper body function, were those who received less than standard primary tumor therapy. It is therefore important to consider whether the offering of less intensive treatment may preserve upper body function at the expense of longer term survival. A recent study by Goodwin and colleagues has documented that older women who receive less than standard breast cancer therapy are at greater risk of dying from their breast cancer than those who receive standard therapy [12]. Furthermore, recent breast cancer mortality trends document that breast cancer mortality has decreased in all age groups except the oldest old, who are also at greatest risk for receiving less than standard treatment [2]. For many older women, the better short-term functional status associated with less intensive treatment may not offset the increased risk of breast cancer mortality.

Our findings must be considered with the study's major limitations in mind. First, we did not measure directly upper body function, either before or after treatment. Second, we did not gather side-specific information, either in relation to handedness or the side on which treatments were performed. Third, we did not collect information about prior recreational or occupational injuries involving the upper extremities. Fourth, our sample was relatively small and the confidence intervals around our estimates of risk are wide. Nonetheless, our data are consistent with the limited number of studies to date and make clinical sense. Whether the early impairments that we have observed will persist awaits the collection of follow-up data.

Given the critical importance of upper body function in maintaining independent living [13], our findings suggest that clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with older women who have early stage breast cancer. For example, women who have cardiopulmonary comorbidity, regardless of the primary therapy that they chose,

are likely to benefit from a supervised rehabilitation program. In addition, women who undergo both modified radical mastectomy and radiation therapy may be another group most likely to benefit from such a program. Finally, we need to design studies to find the best balance between treatment efficacy and functional morbidity for this group of patients.

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Comparison of Interview-Based and Medical-Record Based Indices of Comorbidity Among Breast Cancer Patients

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OBJECTIVES. To compare patient interview-based and medical-record based measures of comorbidity and their relation to primary tumor therapy, all cause mortality, self-reported upper body function, and overall physical function.

METHODS. Three-hundred and three breast cancer patients (≥ 55 years) who were diagnosed in 1 of 5 Boston hospitals were enrolled. Patient interviews and medical record abstracts provided the information necessary to construct the Charlson index, Satariano index, and a new interview-based index of cardiopulmonary comorbidity. Those indices were used alone and in combination to predict the patient outcomes.

RESULTS. The indices of comorbidity corresponded well with one another. No index of comorbidity predicted mortality or receipt of definitive primary therapy. The new interview-based index of cardiopulmonary comorbidity was a better predictor of upper body function and overall physical function than was the interview-based or medical record-based Charlson or Satariano indices of comorbidity.

CONCLUSION. Older breast cancer patients are able to provide information about their diseases and related symptoms that correlates well with medical record-based measures of comorbidity and displays similar patterns of predictive power. A new self-reported measure of cardiopulmonary comorbidity performs better than the medical record-based measures for predicting patient related functional outcomes.

Key words: epidemiologic factors-comorbidity; breast neoplasms. (Med Care 1999;37: 339–349)

Interest in explaining and reducing sources of variation in medical care has burgeoned, fueled by increasing concerns about the costs, quality, and outcomes of care. Critical to the discourse is the accurate measurement of comorbid or co-existent diseases, as they may influence both the processes and outcomes of care. For example, studies conducted throughout the world over the past decade have documented that breast cancer care for women ≥ 65 years differs substantially from that of younger postmenopausal women, with differences being most pronounced between those ≥ 75 years and their younger counterparts.[1–11] Because the questions of interest have been the relationships between age and appropriate breast cancer therapy, as well as between age and mortality, statistical adjustment for comorbidity has been critical. The most popular methods of comorbidity measurement derive from medical-record or claims based counts of medical conditions, with or without weighting for severity. With appropriate treatment as the outcome, comorbidity has failed

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repeatedly to completely explain age-associated variations in treatment.[3,6,8,10,11] Furthermore, comorbidity has been found to vary in its relationship to survival.[6,12–14]

Interest in quality of life outcomes,[15] as well as the recognition that older women represent the largest group of breast cancer survivors[16] have provided new reasons for the accurate measurement of comorbidity in older women. Such measurement can help disentangle the effects of breast cancer treatment from those related to underlying diseases. Although the medical record and claims based approaches have their strengths, they also have important limitations. Medical-record review is costly and concerns about patient confidentiality are beginning to limit investigators' access to medical records. Furthermore, medical records may incompletely capture patient symptoms; this is certainly the case when relying on claims data. Although the claims-based approach is less expensive than medical record review, the rapid migration of older persons into managed care plans that do not submit claims to Medicare increasingly limits its applicability. Finally, claims information is generally insufficient to answer important questions about patterns of care, particularly in relation to treatments not covered by Medicare (eg, tamoxifen) and health outcomes other than mortality.

Because of those limitations, we and others have begun to evaluate the use of interview-based reports of comorbidity.[11,17–20] Studies comparing interview-based versus medical record-based information are promising. In this paper, we compare interview-based and medical-record based measures of comorbidity and their relation to a range of patient outcomes, including primary tumor therapy and all cause mortality, as well as self-reported upper body and overall physical function.

Methods

Sampling

Details of the study have been described elsewhere.[11] We studied women ≥ 55 years of age with newly diagnosed stage I and stage II invasive breast carcinoma who were cared for at 1 of 5 hospitals in Boston, Massachusetts. Women were ineligible if they had a history of another cancer diagnosis within the previous 5 years or had any prior history of breast cancer. Study participants were sent an introductory letter signed by their surgeon and a consent form at approximately 2 to 3 months following definitive surgical treatment. An interviewer further explained the study, answered questions, and obtained informed consent.

Data Collection

Data were collected from patients' medical records and through a 35 minute computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included the following: tumor size, axillary node status, breast surgery or surgeries performed (mastectomy or breast conserving surgery, with or without axillary dissection), receipt of post-operative radiation therapy, and whether the patient had any of a series of specified co-existing conditions: hypertension, congestive heart failure, angina, previous myocardial infarction, emphysema, chronic bronchitis, asthma, stroke, dementia, Parkinson's disease, diabetes mellitus, and thyroid disease. Co-existing conditions other than those specified were also recorded. All information about co-existing conditions was abstracted from surgeons' initial visit notes, that is, before surgical therapy. The patient telephone interview ascertained demographic variables, the SF-36 Health Survey,[21] diagnoses made by a physician of the same specified co-existing conditions collected from the medical records, and symptoms of cardiopulmonary diseases.

Major Analytic Variables

Dependent Variables. Our first dependent variable was a dichotomous variable representing whether or not women received definitive primary tumor therapy for their breast cancer. We defined definitive therapy as modified radical mastectomy or breast conserving surgery with axillary dissection and radiation therapy.[22,23] Our second dependent variable was the time to death from any cause. For this preliminary analysis, we ascertained deaths among the population from reports of next-of-kin and by matching the identification of patients who had been lost to interview follow up against the state's death records through May 14, 1998. For our quality of life outcomes, we considered both a breast cancer-specific as well as a

general measure of physical function. Our breast cancer-specific measure was a dichotomous variable representing decline in upper body function in relation to breast cancer treatment. Patients were classified as having a decline in upper body function in relation to their breast cancer treatment if: 1) they reported having no difficulty in performing any of three tasks requiring upper body function before treatment and reported that any of those tasks were somewhat difficult, very difficult, or that they did not do the task in the four weeks before interview; 2) they reported that performing any of the three tasks requiring upper body function was somewhat difficult before treatment, and reported that the same tasks were very difficult or that they did not do the tasks, in the 4 weeks before interview; or 3) they reported that performing any of the 3 tasks was very difficult before treatment, and that they did not do the same tasks in the 4 weeks before interview. Patients who did not meet any of these classifications were categorized as having no treatment-related decline in upper body function. Our measure of general function was the continuous physical function index (PFI10) from the SF-36 Health Survey,[21] which was administered to patients at their baseline interview.

Independent Variables. We constructed 5 different measures of comorbidity. Table 1 compares the diseases included in each measure. The first index was a self-reported measure of cardiopulmonary comorbidity derived from the Total Illness Burden Index.[17] The larger Total Illness Burden Index includes measures of 15 different disease categories. We chose to assess the subset of cardiopulmonary items because we thought that from a clinical perspective they were most likely to be related to the outcomes of interest. To derive the cardiopulmonary comorbidity score, individual scores are assigned to ischemic heart disease, chronic obstructive pulmonary disease, and congestive heart failure (Fig. 1).

Second, we constructed the Satariano index of comorbidity[12] from the medical record abstract and from the subject's interview. This index includes as comorbid conditions myocardial infarction, other types of heart disease (valvular disease, arrhythmia, and congestive heart failure), diabetes mellitus, other forms of cancer, and respiratory, liver, and gallbladder conditions. The score was then collapsed into categories of 0, 1, 2, or 3+ conditions as described by the developers of the index.[12] Dummy variables representing each nonzero category were included in the multivariate regression models. Our medical record-based Satariano index differed from the original index only in that we did not record histories of other cancers.[12] Women were ineligible for our study if they had a history of another cancer within 5 years of the breast cancer diagnosis and if they had any history of another breast cancer. Our patient interview-based Satariano index did not include diagnoses of gall bladder disease or liver disease because the interview did not ask about those conditions. By medical record review, 27 patients had gall bladder disease and 4 patients had liver disease.

Third, we constructed the Charlson index of comorbidity[13] from the medical record information and from the subject's interview. That index includes as comorbid conditions myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, liver disease, diabetes mellitus, malignancies, and AIDS. Weights are given to conditions with greater severity (eg, diabetes mellitus with end organ damage receives a weight of 2 and moderate or severe liver disease receives a weight of 3). In this scoring scheme, weighted scores were then categorized as 0, 1 to 2, 3 to 4, or 5+, as described by the developers of the index.[13] Dummy variables representing each nonzero category were included in the multivariate regression models. Our medical record-based Charlson index differed from the original index in that we could not include the higher order conditions weighted most heavily by Charlson because we did not collect those measures of severity. Given the nature of the higher order conditions and of the study population, we expect that our approximation would differ little from the Charlson comorbidity index for most subjects. Our subject interview-based Charlson index also did not include dementia, peptic ulcer disease, or liver disease because the interview did not ask about those conditions. By medical record review, 1 patient had dementia, 4 patients had peptic ulcer disease, and 4 patients had liver disease.

Confounding Variables. We included the following potential confounding variables in our multivariate models: age; education ($<$ high school vs. $\geq$ high school); living arrangement (living alone vs. living with one or more household members); marital status (married or living with someone vs. any other); body mass index (BMI,

TABLE 1. Diseases Included in the Cardiopulmonary Comorbidity Index, the Satariano Index of Comorbidity, and the Charlson Index of Comorbidity

Cardiopulmonary Comorbidity Index*	Satariano Index	Charlson Index†
Ischemic heart disease	Myocardial infarction	Myocardial infarction
Congestive heart failure	Other types of heart disease, including congestive heart failure	Congestive heart failure
Chronic obstructive pulmonary diseases	Respiratory conditions, including chronic obstructive pulmonary disease	Chronic pulmonary disease
	Diabetes, cancer (other than index diagnosis)‡	Diabetes
	Gall bladder conditions,§ and liver conditions§	Mild liver disease,# peripheral vascular disease, cerebrovascular disease, dementia# connective tissue disease, and peptic ulcer disease#

* See Figure 1 for a more detailed description of the cardiopulmonary comorbidity index, including a description of its modification by symptoms.

† Only the conditions with a weight of 1 are included in the description. More severe comorbid conditions, which were weighted more heavily by Charlson et al, are not included here.

‡ Not included in the Satariano index derived from medical records in this study.

§ Not included in the Satariano index derived from the patient interview in this study.

Not included in the Charlson index derived from the patient interview in this study.

self-reported weight in kilograms divided by height in meters squared); tumor stage (stage I vs. stage II); primary breast cancer therapy (mastectomy versus breast conserving surgery and radiation therapy, not included when appropriate therapy was the dependent variable); axillary node evaluation (performed or not, not included when appropriate therapy was the dependent variable); and days to baseline interview from date of definitive surgery.

Analytic Strategy

To assess the correspondence between the measures of comorbidity, we calculated the correlation between all possible pair wise combinations of the 5 measures of comorbidity. For this analysis only, the Charlson and Satariano indices were included as continuous measures.

For each dependent variable, we constructed a multivariate model that included the confounding variables. For the dichotomous dependent variables, we used logistic regression as the multivariate technique. For the continuous dependent variable (PFI10), we used linear regression as the multivariate technique. For the survival analysis, we used proportional hazards regression as the multivariate technique. After including the confounding variables, we first added the cardiopulmonary comorbidity variable; we, then, added the cardiopulmonary comorbidity variable in combination with the Satariano or Charlson dummy variables. We determined whether the cardiopulmonary comorbidity variable adequately explained the variance of the dependent variable caused by comorbid disease status by calculating the P value associated with the improvement in model fit engendered by adding the Satariano or Charlson variables. In cases in which the addition of the Satariano or Charlson variables significantly improved the model fit, we compared the standardized coefficients of the cardiopulmonary comorbidity score and an ordinal variable representing the Satariano or Charlson index to determine which measure of comorbidity was the most strong predictor of the dependent variable. We conducted the analysis first with the Charlson and Satariano indices derived from the medical record and then repeated the analysis with those indices derived from the subject interviews.

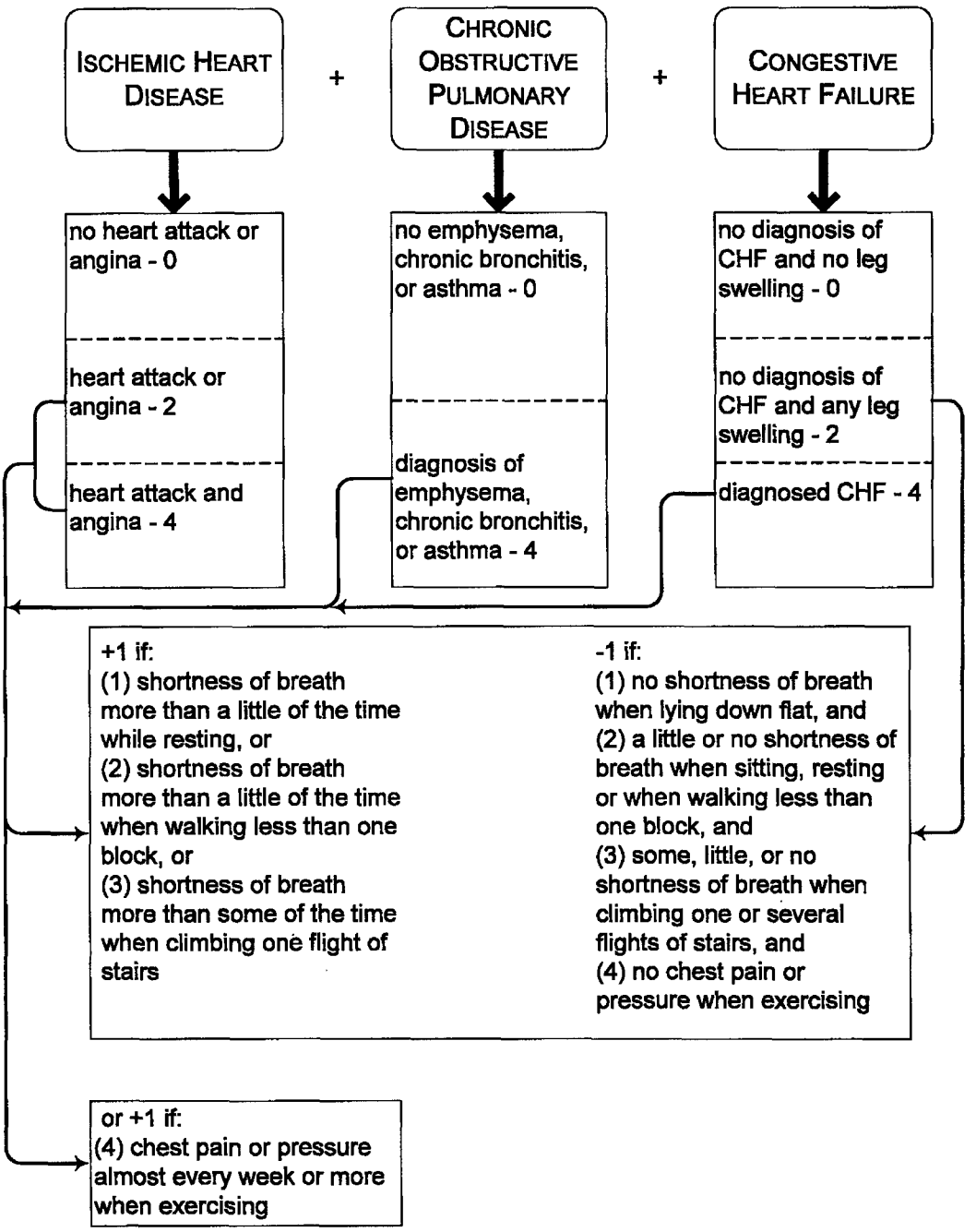

FIG. 1. Derivation of the cardiopulmonary comorbidity score from patient interview responses.

Results

We enrolled 303 patients during the study period (Table 2). Most of the women (83%) had at least a high school education. Two thirds of the women had stage-I breast cancer, the rest had stage-II disease. The majority of the women (64%) received breast conserving surgery and radiation therapy for their primary treatment, and 85% had an axillary node dissection. Three quarters of the

TABLE 2. Distributions of Patient Characteristics

Characteristic	Number	Percent
Age at diagnosis		
55–64	126	41.6
65–74	111	36.6
75+	66	21.8
Education		
<12 years	51	17.0
≥12 years	249	83.0
Living arrangement		
Alone	103	34.3
With 1 or more	197	65.7
Marital status		
Married or living with someone	148	49.2
All other	152	50.8
Body mass index (kg/m^2)		
≤23	91	30.5
>23 to ≤27.5	120	40.3
>27.5	87	29.2
Breast cancer stage		
Stage I	193	63.9
Stage II	109	36.1
Axillary node dissection		
Yes	258	85.4
No	44	14.6
Primary tumor therapy		
Breast conserving surgery and radiation therapy	195	64.3
Mastectomy	71	23.4
Other	37	12.2
Radiation therapy		
Yes	206	68.0
No	97	32.0
Appropriate therapy		
Yes	234	77.2
No	69	22.8
Days between definitive surgery and interview		
1–100	28	9.2
101–130	138	45.5
131–160	74	24.4
>161	63	20.8
Upper body function decline		
Yes	106	35.6
No	192	64.4
Physical function index (scaled 0–100)		
0–25	13	4.4
26–50	37	12.4
51–75	86	28.4
76–100	162	53.5
Vital status		
Died from breast cancer	13	4.3
Died from other than breast cancer	5	1.7
Death certificate not located	6	2.0
Alive	279	92.1

cases met our standards for definitive primary tumor therapy. Most (75%) of the baseline interviews occurred between 100 and 160 days after the patient's definitive surgery.

About one third of the patients suffered some decline in upper body function by the date of their interview. Seventeen percent scored below 50, on a scale from 0 to 100, on the SF-36 Health Survey index of physical function. We located death certificates for 18 of 24 patients lost to follow up as a result of death. Thirteen of 18 deaths were attributed to the patient's breast cancer on the death certificate.

The average of the interview-based comorbidity score increased regularly as the Charlson and Satariano indices increased (Table 3), indicating good correspondence on average between those 3 methods of rating the patient's comorbid disease status. The correspondence held whether the Charlson and Satariano indices were derived from medical records or from subject interviews. The pair-wise correlations between the continuous measures of each comorbidity index further demonstrates the correspondence (Table 4). The correlation coefficient of the cardiopulmonary comorbidity index with the medical record Charlson index was 0.45 ($P \leq 0.001$), with the medical record Satariano index was 0.52 ($P \leq 0.001$), with the patient interview Charlson index was 0.75 ($P \leq 0.001$), and with the patient interview Satariano index was 0.73 ($P \leq 0.001$). Although those measures of comorbidity are highly correlated, the correlations between the continuous measure of cardiopulmonary comorbidity index and the categories of the Charlson or Satariano indices are not

TABLE 3. Relationships between the Charlson and Satariano Indices and Interview-Based Index of CC

	CC Mean ± SD	CC SEM	Range of CC	Number of Subjects
Satariano index group				
Medical record derived				
Zero	0.74 ± 1.44	0.10	0–8	205
One	2.21 ± 2.80	0.32	0–13	77
Two	4.89 ± 3.31	0.78	0–10	18
Three or more	10.00 ± 8.66	5.00	0–15	3
Satariano index group				
Patient interview derived				
Zero	0.49 ± 1.04	0.07	0–6	225
One	3.37 ± 2.64	0.34	0–10	59
Two	6.44 ± 3.68	0.87	1–15	18
Three or more	15		15	1
Charlson index group				
Medical record derived				
Zero	0.91 ± 1.80	0.12	0–13	237
One or two	3.08 ± 3.04	0.39	0–11	62
Three or four	8.50 ± 7.68	3.84	0–15	4
Five or more				0
Charlson index group				
Patient interview derived				
Zero	0.38 ± 0.81	0.06	0–5	214
One or two	3.61 ± 2.70	0.29	0–11	85
Three or four	12 ± 3.61	2.08	8–15	3
Five or more	15		15	1

CC, cardiopulmonary comorbidity; SEM, standard error of mean.

so strong so as to prevent including both the CC index and the categories of either the Charlson or Satariano index simultaneously in a multivariate model.

Table 5 shows the predictive power of the cardiopulmonary comorbidity measure for each of the dependent variables. In addition, it shows the *P* value associated with the improvement in the model fit contributed by the categorized Charlson or Satariano comorbidity index in combination with the cardiopulmonary comorbidity measure. The measures of association between each index of comorbidity and each dependent variable, as well as the standardized coefficients, are available from the authors.

The cardiopulmonary measure of comorbidity did not predict the receipt of definitive therapy. Furthermore, none of the other 4 measures of comorbidity added significant predictive power to the model.

Perhaps because of the short follow-up time and our inability to segregate decedents by cause of death, none of the measures of comorbidity predict mortality. Furthermore, a follow-up will likely yield sufficient numbers of decedents to allow a more thorough examination of those relationships.

The interview-based cardiopulmonary comorbidity measure did predict upper body dysfunction. None of the other 4 measures of comorbidity added significant predictive power to the model after the cardiopulmonary comorbidity score was included.

Finally, the interview-based cardiopulmonary comorbidity measure strongly predicted the physical function subscale of the SF36 when entered in the multivariate models. The negative coefficients shown in Table 5 for the physical function index indicate that increasing cardiopulmonary comorbidity is associated with declining physical function. All comorbidity measures, except for the

TABLE 4. Correlation Coefficient (*P* value) Between Pair-Wise Combinations of the Continuous Indices of Comorbidity

	Cardiopulmonary Comorbidity	Medical Record Charlson	Medical Record Satariano	Patient Interview Charlson	Patient Interview Satariano
Cardiopulmonary	1.0	0.45	0.52	0.75	0.73
Comorbidity	—	(≤0.001)	(≤0.001)	(≤0.001)	(≤0.001)
Medical record		1.0	0.68	0.58	0.58
Charlson		—	(≤0.001)	(≤0.001)	(≤0.001)
Medical record			1.0	0.55	0.60
Satariano			—	(≤0.001)	(≤0.001)
Patient interview				1.0	0.87
Charlson				—	(≤0.001)
Patient interview					1.0
Satariano					—

medical-record derived Satariano index, significantly improved the model fit when added to the multivariate model that included the cardiopulmonary comorbidity score. This observation suggests that the cardiopulmonary comorbidity index did not fully explain the relation between increasing comorbidity and declining function. In each model, though, the standardized coefficient of the cardiopulmonary comorbidity score indicated that it was a more powerful predictor than the Charlson or Satariano indices, regardless of whether they derived from the medical record or from the patient interview (data not shown, but available from the authors upon request). Therefore, if one could choose only a single measure of comorbidity to predict physical function, the cardiopulmonary comorbidity index would be preferred, at least, in this population.

Discussion

In this comparison of various methods and sources of comorbidity measurement, we found that, regardless of the method or source, no measure of comorbidity was statistically significantly associated with the receipt of definitive primary tumor therapy. In other studies the observed relationship between comorbidity and primary tumor therapy has varied. Although Greenfield et al found that comorbidity and age were independently and significantly associated with definitive treatment among women 50 years or older,[3] Bergman found that advanced age (≥ 75 years) was a better predictor of treatment than was comorbidity.[6] Both studies relied on medical record-based measures of comorbidity. Similarly, in studies using claims-based Charlson indices, Newschaffer et al found that comorbidity had no relationship to surgical or radiation therapy,[10] whereas Ballard-Barbash found modest relationships between comorbidity and both surgical and radiation therapies after controlling other potentially confounding factors.[8] In both the Newschaffer and Ballard-Barbash studies, patients in the oldest age groups were less likely to receive these therapies, independent of all other measured variables.[8,10]

Although it is not central to this investigation, our findings and those of others lead us to conclude that considerations of comorbidity do not completely drive therapeutic decisions regarding primary tumor therapy and do not explain the relationship between age and treatment patterns, regardless of the method of comorbidity measurement. Nonetheless, adequate measurement of comorbidity should be required of all studies of age associated variations in breast cancer care. Here adequacy of measurement should be defined in terms of the risks and benefits of therapy. Thus, a measure of cardiopulmonary comorbidity may well be adequate for studies of surgical and/or radiation therapy. However, studies of adjuvant chemotherapy would need to include laboratory measures of renal and hepatic function.

Although attention to the measurement of comorbidity is important in studies of age-associated

TABLE 5. Relationships Between the Dependent Variables and the Index of Cardiopulmonary Comorbidity, Controlling for the Charlson or Satariano Index of Comorbidity

Dependent Variable	Model	Relative Risk or Change in PFI10 Associated With a Unit Increase in CC (95% CI)	*P* Value Associated With Addition of Charlson or Satariano Index
Receipt of less than appropriate primary tumor therapy	CC alone	1.03 (0.91, 1.16)	Not applicable
	CC + MR* Charlson	0.97 (0.85, 1.11)	0.10
	CC + MR Satariano	1.02 (0.88, 1.17)	0.94
	CC + PI† Charlson	0.98 (0.81, 1.19)	0.24
	CC + PI Satariano	0.93 (0.78, 1.12)	0.39
All cause mortality	CC alone	0.84 (0.65, 1.09)	Not applicable
	CC + MR Charlson	0.84 (0.64, 1.11)	0.95
	CC + MR Satariano	0.85 (0.64, 1.12)	0.98
	CC + PI Charlson	0.84 (0.60, 1.17)	0.99
	CC + PI Satariano	0.89 (0.64, 1.24)	0.78
Upper body dysfunction	CC alone	1.16 (1.04, 1.30)	Not applicable
	CC + MR Charlson	1.13 (0.99, 1.27)	0.18
	CC + MR Satariano	1.14 (1.00, 1.31)	0.34
	CC + PI Charlson	1.12 (0.95, 1.33)	0.39
	CC + PI Satariano	1.14 (0.97, 1.34)	0.20
Physical function index (PFI10)	CC alone	−2.56 (−3.43, −1.68)	Not applicable
	CC + MR Charlson	−2.26 (−3.23, −1.30)	0.001
	CC + MR Satariano	−2.65 (−3.68, −1.62)	0.142
	CC + PI Charlson	−2.41 (−3.78, −1.04)	0.063
	CC + PI Satariano	−2.75 (−4.03, −1.48)	0.002

CC, cardiopulmonary comorbidity index.
* MR, derived from the patient's medical record.
† PI, derived from the patient's interview.

variations in breast cancer care, equal attention should be given to alternative explanations. For example, a patient's functional status is likely to be important, because comorbidity and functional status are known to contribute unique information to our understanding of the health status of older persons.[24–26] However, studies that have controlled for functional status, either based on medical record information[3] or patient's self report[11] have found that age persists as an independent predictor of treatment. The lack of association may reflect the need for more detailed measures of functional status, and further studies are needed that measure functional status more comprehensively. Additional studies are also needed to more adequately explore the roles of physician attitudes and fully informed patient preferences as predictors of treatment.

With respect to mortality, none of our comorbidity measures was associated; that may be because the number of deaths in our sample is, as yet, small. Newschaffer et al recently compared Medicare claims versions of the Charlson and Satariano indices with their medical record-based versions in a sample of women (≥ 67 years) who were newly diagnosed with breast cancer. Although the claims-based and medical record-based methods had poor agreement, indices derived from both sources were modestly (odds ratios of 1.28–1.53) associated with 3 to 5 year all cause mortality, controlling for age, stage, and treatment. The Charlson claims-based score added modest prediction over the Charlson medical record-based score.[6]

Finally, we found that patient self-report of cardiopulmonary comorbidity was a better predic-

tor of breast cancer specific as well as general physical function than were either the medical record- or patient interview-based Satariano and Charlson indices. The fact that neither the medical-record nor patient-interview based Satariano and Charlson measures performed as well suggests that the observed relationships are not caused by measurement source (ie, medical record vs. patient). In cases in which symptoms reflect disease severity, patients may be a better source of information than their physicians. Indeed, in comparison with patients' report of cardiopulmonary comorbidity, both the Satariano and Charlson, regardless of source, underestimated comorbidity 32% to 34% of the time. This may partially be because neither method takes into account the contribution of symptoms. For example, in the Charlson index, severe pulmonary and cardiac disease receive the same weighting as do mild forms of these diseases.[13]

Studies comparing medical records and patient self report suggest that patients are most accurate when asked about well defined conditions, such as heart disease or diabetes mellitus and least accurate for less well defined conditions such as arthritis.[17,18] Older age and less education have been variably associated with lower agreement between medical records and self report.[18–20] Thus, studies in which well defined diseases are critical and/or in which patient symptoms are relevant, patient self reports of diseases and symptoms may be sufficient, if not superior, for the measurement of comorbidity. That approach may be particularly useful in circumstances in which missing data in medical records are common.

Although our findings are promising, they must be viewed with several limitations in mind. First, the women in our study were mostly White and well educated. Nonetheless, they ranged in age up to 97, so included women at greatest risk for a large burden of comorbid conditions. Second, we did not construct our data collection instruments to fully represent the Satariano and Charlson indices. Thus, some of the underestimation of those measures may be related to incomplete data collection. The medical record-based Charlson index consistently underestimated diagnoses as identified by a complete ascertainment through patient interview in a similar study.[20] The interview-based Charlson and Satariano indices may, therefore, balance the incomplete assessment of diseases with a more complete ascertainment of the diseases that were assessed. Third, our sample size was relatively small and resulted in imprecise estimates of effect. Fourth, the small number of deaths preclude definitive statements about the relationship between our various comorbidity measures, and all cause mortality.

Nonetheless, we believe that our data support several conclusions. First, older breast cancer patients are able to provide information about their diseases and relate symptoms that correlate well with medical record-based measures and displays similar patterns of predictive power. Second, our self-reported measure of cardiopulmonary comorbidity performs better than our medical record-based measures in the prediction of patient-related functional outcomes. Continued refinement of this approach offers promise for the efficient and valid measurement of comorbidity.

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The Care of Older Women With Early-Stage Breast Cancer

What Is the Role of Surgeon Gender?

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BACKGROUND. Over the past decade and a half, a substantial literature has documented age-dependent variations in breast cancer care. Accumulating evidence suggests that these variations impact the health outcomes of older women with breast cancer. Surgeon gender may be an important source of age-dependent variations in care.

OBJECTIVE. To examine the relationship between surgeon gender and primary tumor therapy and systemic adjuvant therapy among 303 older women with early-stage breast cancer cared for by 20 surgeons in Boston, Massachusetts.

METHODS. The research design was a cross-sectional observational study. The subjects were women at least 55 years of age with newly diagnosed Stage I or II breast cancer. The main outcome measure was definitive primary tumor therapy and systemic adjuvant therapy.

RESULTS. After adjustment for patient and tumor characteristics, patients of female surgeons were more likely to receive definitive treatment, with the strongest effect being observed for the receipt of both definitive primary tumor therapy and systemic adjuvant therapy (odds ratio 4.5; 95% confidence interval 2.7, 7.7).

CONCLUSIONS. Women with early-stage breast cancer cared for by female surgeons are more likely to receive standard therapies. Surgeons provide the initial care, both diagnostic and therapeutic, for all women with breast cancer. Their role in breast cancer care is pivotal and has a substantial impact on the nature of breast cancer care received.

Key words: breast cancer; older women; surgeon gender; treatment. (Med Care 1999;37: 1057–1067)

Over the past decade and a half, a substantial literature has documented age-dependent variations in breast cancer care.[1–13] Although some aspects of care have changed over this period of time (eg, breast conserving surgery has increased), age-dependent variations have persisted into the 1990s.[13] The next-level questions are these: (1) Do these variations make a difference with respect to important health outcomes? (2) If so, what are the reasons for these variations?

Accumulating observational evidence, albeit incomplete, suggests that age-dependent variations do impact the health outcomes of older women with breast cancer. Specifically, studies from the United States and Italy have identified both higher recurrence rates and higher mortality rates among

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women who receive less than definitive primary tumor therapy.[14–16] Furthermore, breast cancer–specific mortality rates are declining among women younger than 70 years old but are either stable (age range, 70–79 years) or increasing (age range, >80 years) among those 70 years of age or older.[17] Increasing rates of screening mammography and better treatment regimens may partially explain the declining mortality rates among women younger than 70 years old. Although screening mammography rates decline progressively with age, there is no evidence to suggest that the diagnosis of late-stage disease among the oldest women has been increasing over time or that there have been systematic changes in the attribution of breast cancer as the cause of death.[17] This leaves the receipt of less than definitive treatment as the better explanation for why mortality rates among older women are increasing, particularly among those aged 80 years or older.[17] This contention is supported by the available age-specific clinical trial data that fail to demonstrate that treatment efficacy is modified by age.[18–20]

The quality of the medical encounter may be an important source of age-dependent variations in breast cancer care. Studies of physician-patient interactions have demonstrated that the quality of these interactions decreases with patient age. Physicians spend less time with their older patients than they do with their younger patients.[21,22] Physicians also provide better information and support to their younger patients than to their older patients.[23] These physician behaviors are compounded by the behaviors of older patients themselves. In general, older patients are less assertive and defer more to their physicians than do younger patients.[24] Indeed, a recent study of over 1,000 women with breast cancer found that 48% of women ≥70 years of age preferred to have a passive role in decision making, compared with 36% of those 50 to 69 years, and 21% of those <50 years of age.[25]

Gender issues may accentuate the effects of these age-related behaviors. Because of gender disparities in life expectancy, most older patients are women. Until recently, most physicians were men. The latter circumstance is changing rapidly, and a growing literature has documented differences between male and female physicians, both in their styles of interactions and in the care that they deliver. For example, compared with male physicians, female physicians ask more questions and give more information.[26] The longest visits are between female physicians and their female patients; the shortest visits are between male physicians and their female patients.[26] Although several studies have shown that women are more likely to undergo cervical and breast cancer screening if they see female rather than male physicians,[27–29] no study has shown that breast cancer care is similarly influenced.

As part of a study of age-related variations in breast cancer care,[13] we examined the relationship between surgeon gender and primary tumor therapy and systemic adjuvant therapy among older women with early-stage breast cancer cared for by 7 female surgeons and 13 male surgeons in Boston, Massachusetts. We sought to determine whether surgeon gender was associated with the receipt of primary tumor and systemic adjuvant therapy, after relevant patient and physician characteristics had been considered.

Methods

Data Collection

The study's methods have been described elsewhere.[13] Participating women were at least 55 years old and were newly diagnosed with Stage I or II breast cancer. They received their initial breast cancer care from surgeons in office-practice settings affiliated with one of five academic medical centers in Boston, Massachusetts. These settings included general surgery private practices and interdisciplinary breast health care centers. Data were collected from women's medical records, a 35-minute computer-assisted telephone interview with consenting women, and the Massachusetts Physician Profiles database of the Board of Registration in Medicine of the Commonwealth of Massachusetts.[30] Data collected from medical records included stage, estrogen receptor status, surgical procedures performed, and additional therapies received (radiation therapy, chemotherapy and/or hormonal therapy). Medical records were monitored for 6 months to determine whether radiation therapy and chemotherapy were initiated and completed or discontinued, and whether hormonal therapy was initiated. The patient telephone interview included questions about sociodemographic characteristics (age, race, marital status, education, and income); general health-related quality of life; the presence of

physician-diagnosed cardiopulmonary diseases and the frequency of associated symptoms; and ratings of aspects of physician-patient interactions. We obtained training information about surgeons from the Massachusetts Physician Profiles database,[30] including year graduated from medical school, board certification in general surgery, and fellowship training in surgical oncology.

Major Analytic Variables. Our dependent variable had two components: (1) definitive primary tumor therapy, categorized as "yes" if the patient received either modified radical mastectomy or breast-conserving surgery with axillary dissection followed by radiation therapy, otherwise "no"; and (2) systemic adjuvant therapy, categorized as "yes" if the patient received chemotherapy or hormonal therapy either alone or in combination, otherwise "no." These two components were then combined to form a four-level variable: no/no, no/yes, yes/no, and yes/yes, reflecting the receipt of various combinations of definitive primary tumor therapy and systemic adjuvant therapy.

Our independent variable of interest was surgeon gender (female/male). We considered as covariates (1) patient characteristics that have previously been shown to be associated with treatments received by older women with newly diagnosed early-stage breast cancer: age,[1–13] race,[31] marital status,[13] socioeconomic status (education and income),[7,31] comorbidity,[2,6,8] functional status,[2] and physician-patient communication[13]; (2) clinically important prognostic factors that should influence treatment decisions: tumor characteristics (stage [I/II]), estrogen receptor status (positive/negative), and risk of recurrence; and (3) surgeon characteristics that might explain the relationship between surgeon gender and treatment received: years since graduation from medical school (≤15 years/>15 years) and whether they practiced at a breast health center (yes/no). Patients' demographic characteristics included age (55–64, 65–74, 75–84, and ≥85 years), marital status (single, married, widowed, separated, or divorced), education (<high school, high school, some college, and college graduate), and annual household income (≤$14,999, $15,000–$29,999, $30,000– $49,999, and ≥$50,000). We measured comorbidity using patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease, and related disease manifestations and symptoms that were part of the Total Illness Burden Index.[32] We assessed physical function using the ten-item physical function subscale of the Medical Outcomes Study Short Form-36 (SF-36), which is scaled from 0 to 100 with a higher score indicating better function.[33] In the analysis we also considered comorbidity and physical function as four-level ordinal variables, dividing the sample into four approximately equal groups. We categorized node-negative women as being at low, intermediate, or high risk of recurrence based on tumor size and estrogen receptor status,[34] and node-positive women as being at high risk of recurrence. Our measure of patients' perceptions of their own abilities to communicate with their physicians was a three-item scale, developed for this study,[13,35] based on patients' ratings of their abilities to get information from their physicians and give information to them (Cronbach's $\alpha = 0.96$).

Statistical Analysis

We obtained descriptive statistics on all medical record and patient interview variables and then examined the association between the independent variable and covariates, and between these variables and the outcome variable, using analysis of variance and the χ^2 test. Variables that were statistically significantly associated with the dependent variable ($P < 0.05$) at the bivariate level were candidates for entry into a polytomous logistic regression model, a generalization of the binary logistic regression model to more than two outcome categories.[36] Because of cells with zero frequency, we recategorized age as 55 to 64, 64 to 74, and ≥75 years and education as <high school, high school, and >high school for this analysis. Income was not retained in the final model because neither its presence nor its absence substantially changed the parameter estimate associated with surgeon gender, most likely because of its strong association with age, marital status, and education (all $P = 0.001$).

The polytomous logistic regression model assumes that the outcome variable categories are mutually exclusive. The odds ratio for the independent variable (surgeon gender) at a given outcome level (eg, yes/yes) represents the odds of receiving yes/yes over receiving no/no among patients cared for by female surgeons compared with those cared for by male surgeons.[37] In choosing this analytic strategy, we were concerned about violating the statistical assumption of indepen-

dence. To address this concern, we examined the correlation among patients within surgeon, and the observed correlation coefficients were very small (eg, 0.00, -0.03, 0.04) suggesting that the assumption of independence in the polytomous regression model is valid. We were also concerned that the results observed might reflect 1 or 2 surgeon outliers. When we examined the distribution of treatments by surgeon, not only were there no outliers, but the distributions of treatments were similar within female and male surgeon groups

Finally, we also performed a series of stratified analyses to assess whether the treatment patterns represented potential overtreatment or undertreatment. In these analyses we examined patterns of care in relation to risk of recurrence by surgeon gender.

Results

Study Sample

Three hundred three women participated in the study. A little more than half (58%) of our subjects were ≥65 years of age (range, 55–97 years), and most were white (93%). About half were married (51%), and the majority had a high school education or more (83%). Their average comorbidity score was 7.06 (range, 3–20). The majority of patients had Stage I disease (64%). The majority of women in our study also underwent breast-conserving surgery and axillary dissection followed by radiation therapy (56%); fewer than a quarter received a modified radical mastectomy (22%); the remaining 22% received other therapies. About two thirds (67%) of the women received some form of systemic adjuvant therapy. Of those, most (76%) received hormonal therapy alone. A much smaller percentage received either chemotherapy alone (13%) or both chemotherapy and hormonal therapy (11%).

The Massachusetts Physician Profiles database provided information about 19 of 20 surgeons. These surgeons, including 7 women and 12 men, cared for 301 of 303 patients. A little over half (53%) had graduated from medical school within the past 15 years. All but 1 were board certified in general surgery. Two female surgeons and 2 male surgeons had completed surgical oncology fellowship training.

Patient Characteristics in Relation to Surgeon Gender

Patient characteristics in relation to surgeon gender are shown in Table 1. As can be seen, the patients cared for by female surgeons were very similar to those cared for by male surgeons with respect to demographic characteristics, health status, tumor characteristics, and ability to communicate with their physicians. However, male surgeons did care for a higher proportion of women of minority status and those with the lowest income.

Patient and Surgeon Characteristics in Relation to Therapies Received

Patient and surgeon characteristics in relation to therapies received are shown in Table 2. Women <65 years of age were more likely to receive both definitive primary therapy and systemic adjuvant therapy (yes/yes). Women ≥85 years of age were more likely to receive neither definitive primary therapy nor systemic adjuvant therapy (no/no). No differences were observed as a function of race, although the number of nonwhite women (n = 20) was quite small. Married women, those who were college educated, and those with an annual household income of ≥$30,000 were more likely to receive both definitive primary therapy and systemic adjuvant therapy than those who were not married, had less education, or had lower annual household incomes, respectively. There were no significant differences in treatments received with respect to cardiopulmonary comorbidity or physical function. As expected, women with Stage II disease and those who were at higher risk of recurrence were much more likely to receive both definitive primary therapy and systemic adjuvant therapy. However, there were no differences in relation to estrogen receptor status.

There were no significant differences in treatments received related to women's perceptions of their ability to communicate with their physicians. In addition, no differences were observed with respect to years since the surgeons had graduated from medical school or whether they worked in a breast health care center. However, women cared for by female physicians were more likely to receive both definitive primary therapy and systemic adjuvant therapy, whereas women cared for by male physicians were more likely to receive neither.

TABLE 1. Patient Characteristics and Surgeon Gender

Patient Characteristics	Surgeon Gender: Female (n = 174)	Surgeon Gender: Male (n = 129)	P Value
Patient demographics			
Age (years)			
55–64	75 (60%)	51 (40%)	0.74
65–74	65 (59)	46 (41)	
75–84	27 (52)	25 (48)	
85+	7 (50)	7 (50)	
Race			
White	168 (60)	113 (40)	0.001
Non-White	4 (20)	16 (80)	
Marital status			
Married	84 (57)	64 (43)	0.94
Widowed	56 (57)	43 (43)	
Single/Divorced	32 (59)	22 (41)	
Education			
<High school	26 (51)	25 (49)	0.65
High school	61 (57)	46 (43)	
Some college	45 (63)	27 (47)	
College graduate	40 (57)	30 (43)	
Income*			
≤$14,999	26 (49)	27 (51)	0.018
15,000–29,999	44 (73)	16 (27)	
30,000–49,999	40 (63)	24 (37)	
50,000+	30 (57)	23 (43)	
Health status			
Comorbidity score			
I (lowest quartile)	51 (58)	37 (42)	0.53
II	45 (64)	25 (36)	
III	41 (55)	34 (45)	
IV (highest quartile)	37 (53)	33 (47)	
Physical function score			
I (lowest quartile)	39 (50)	39 (50)	0.18
II	31 (53)	27 (47)	
III	39 (59)	27 (41)	
IV (highest quartile)	63 (66)	33 (33)	
Tumor characteristics			
Stage			
I	114 (59)	79 (41)	0.41
II	59 (54)	50 (46)	
Risk of recurrence			
Low	42 (67)	21 (33)	0.24
Intermediate	63 (58)	45 (42)	
High	51 (53)	45 (47)	
Communication skills	70.43	70.98	0.86

*Values missing for 73 subjects.

TABLE 2. Patient and Surgeon Characteristics and Therapies Received: Definitive Primary/Systemic Adjuvant*

Characteristics	No/No (n = 22)	No/Yes (n = 47)	Yes/No (n = 77)	Yes/Yes (n = 157)	P Value
Patient demographics					
Age (years)					
55–64	5 (4%)	8 (6%)	35 (28%)	78 (62%)	0.001
65–74	8 (7)	10 (9)	28 (25)	65 (59)	
75–84	4 (8)	23 (44)	11 (21)	14 (27)	
85+	5 (36)	6 (43)	3 (21)	0 (00)	
Race					
White	20 (7)	41 (14)	72 (26)	148 (53)	0.55
Non-White	2 (10)	5 (25)	5 (25)	8 (40)	
Marital status					
Married	6 (4)	12 (8)	44 (30)	86 (58)	0.001
Widowed	13 (13)	22 (22)	18 (18)	46 (47)	
Single/Divorced	3 (6)	12 (22)	15 (28)	24 (44)	
Education					
<High school	10 (20)	11 (21)	10 (20)	20 (39)	0.002
High school	8 (5)	14 (13)	26 (24)	59 (55)	
Some college	0 (0)	12 (17)	26 (36)	34 (47)	
College graduate	4 (6)	8 (12)	15 (21)	43 (61)	
Income†					
≤$14,999	7 (13)	17 (32)	12 (23)	17 (32)	0.001
15,000–29,999	5 (8)	4 (7)	19 (32)	32 (53)	
30,000–49,999	0 (0)	5 (8)	15 (23)	44 (69)	
50,000+	2 (4)	5 (9)	12 (23)	34 (64)	
Patient health status					
Comorbidity score					
I (lowest quartile)	4 (5)	15 (17)	22 (25)	47 (53)	0.8
II	4 (6)	10 (14)	19 (27)	37 (53)	
III	7 (8)	9 (12)	16 (21)	43 (57)	
IV (highest quartile)	7 (10)	13 (19)	20 (28)	30 (43)	
Physical function score					
I (lowest quartile)	7 (9)	15 (19)	17 (22)	39 (50)	0.2
II	7 (12)	10 (17)	13 (22)	28 (42)	
III	3 (5)	11 (17)	19 (29)	33 (50)	
IV (highest quartile)	4 (4)	7 (7)	28 (29)	57 (59)	
Tumor characteristics					
Stage					
I	20 (10)	40 (21)	64 (33)	69 (36)	0.001
II	2 (2)	7 (6)	13 (12)	87 (80)	
Estrogen receptor status					
Positive	12 (6)	34 (16)	48 (23)	116 (55)	0.44
Negative	5 (8)	6 (9)	19 (28)	37 (55)	

(Continues)

TABLE 2 (Cont.)

Characteristics	No/No (n = 22)	No/Yes (n = 47)	Yes/No (n = 77)	Yes/Yes (n = 157)	P Value
Risk of recurrence					
Low	5 (8)	13 (21)	26 (41)	19 (30)	0.001
Intermediate	7 (6)	18 (17)	24 (22)	59 (55)	
High	4 (4)	7 (7)	14 (15)	71 (74)	
Communication skills	69.44	66.88	70.67	72.24	0.57
Surgeon characteristics					
Years since medical school graduation					
≤15 years	15 (7)	34 (16)	52 (25)	106 (51)	0.95
>15 years	7 (7)	13 (14)	25 (26)	49 (52)	
Gender					
Female	7 (4)	27 (16)	42 (24)	98 (56)	0.05
Male	15 (12)	20 (15)	35 (27)	59 (46)	
Practice site					
Breast health center	17 (8)	35 (17)	49 (23)	111 (52)	0.47
Other	5 (5)	12 (13)	28 (31)	46 (51)	

*No/No, no definitive primary tumor therapy; No/No, no systemic adjuvant therapy; No/Yes, no definitive primary tumor therapy, systemic adjuvant therapy; Yes/No, definitive primary tumor therapy, no systemic adjuvant therapy; Yes/Yes, definitive primary tumor therapy, systemic adjuvant therapy.

†Values missing for 73 subjects.

The results of our polytomous regression model are shown in Table 3. In each comparison with the referent outcome group (neither definitive primary tumor therapy nor systemic adjuvant therapy) and controlling for age, stage, education, and marital status, the odds of receiving each of the more definitive treatment combinations were statistically significantly greater among women cared for by female surgeons than among women cared for by male surgeons, with the strongest effect being observed for the receipt of both definitive primary therapy and systemic adjuvant therapy. Patients cared for by female surgeons were about 4.5 times more likely to receive both therapies than were those cared for by male surgeons.

With respect to the question whether these patterns may represent overtreatment or undertreatment, among patients of female surgeons, 60% of those who received neither definitive primary tumor therapy nor adjuvant therapy were at low risk of recurrence. Among patients of male surgeons, 18% of those who received neither definitive primary tumor therapy nor adjuvant therapy were at low risk of recurrence. In contrast, *no* patients of female surgeons who received neither therapy were classified as being at high risk of recurrence, whereas 36% of patients of male surgeons who received neither therapy were at high risk.

Conclusions

In this study of breast cancer care received by older women, we found that surgeon gender was independently associated with the receipt of definitive primary tumor therapy and systemic adjuvant therapy. Our data do not support the contention that the observed relationship is because different kinds of women seek care from female surgeons than seek care from male surgeons (Table 1). In addition, treatment patterns do not differ according to comorbidity and functional status, or in relation to women's perceptions of their ability to communicate with their physicians, the recency of their surgeon's training, or the setting in which

TABLE 3. Polytomous Logistic Regression* Predicting Receipt of Primary Tumor Therapy and Systemic Adjuvant Therapy†, ‡

Characteristics	No/Yes OR* (95% CI)	Yes/No OR* (95% CI)	Yes/Yes OR* (95% CI)
Surgeon gender			
Female	3.1 (1.8, 5.5)	2.7 (1.6, 4.7)	4.5 (2.7, 7.7)
Male	—1.0—	—1.0—	—1.0—

*Receipt of neither therapy (No/No) is the referent group.

†Adjusted for age, stage, education, and marital status.

‡No/Yes, no definitive primary tumor therapy, systemic adjuvant therapy; Yes/No, definitive primary tumor therapy, no systemic adjuvant therapy; Yes/Yes, definitive primary tumor therapy, systemic adjuvant therapy.

care is delivered (Table 2). Furthermore, in our polytomous logistic regression analysis (Table 3), the effect of surgeon gender persisted after statistical control for patient age, education, marital status, and tumor stage. Although it is possible that unmeasured factors may be unbalanced across groups of women cared for by female as opposed to male surgeons, this seems unlikely.

Nonetheless, our findings must be interpreted with the study's limitations in mind. First, our older women with breast cancer were mostly middle-class white women from one city in the northeastern United States, and the oldest women (≥85) were under-represented because of a higher refusal rate.[13] Second, these women were cared for by a relatively small number of surgeons who practiced in settings with academic affiliations. Although we cannot be certain, it is possible that the variations we observed might have been greater had we studied a more diverse group of women and surgeons. Third, we did not have detailed information about actual clinical encounters between surgeons and patients. This precluded our developing an in-depth understanding of the factors that explain the observed relationship between surgeon gender and therapies received.

In the absence of such information, we suggest the following as a possible explanation of our findings. The lack of an association between comorbidity and therapies received, which has been observed by others,[2,6,8,10,13] in conjunction with the similar lack of association between recency of surgeon training, site of care, and therapies received contradict conventional wisdom. When coupled with the observation that therapies received do vary in relation to surgeon gender, however, they suggest that female and male surgeons may interpret differently the available literature regarding treatment efficacy and effectiveness. We believe that female surgeons may weigh the evidence more carefully and discuss it more comprehensively with their patients. Rather than deciding what is best for patients and making assumptions about the importance of factors such as risk of recurrence, out-of-pocket expenses, and difficulty getting to and from treatments,[13] female surgeons may explore more explicitly the weight that women give to these considerations.

In spite of observational study evidence linking variations in primary tumor therapy and patient outcomes, there is considerable controversy surrounding what constitutes appropriate therapy for older women with breast cancer. Radiation therapy following breast-conserving surgery is one example. Clinical trials have consistently demonstrated that radiation therapy following breast-conserving surgery reduces local recurrence rates by about 20%, regardless of stage.[19,38] Advocates of omitting radiation therapy in older women who undergo breast-conserving surgery argue that clinical trials have not demonstrated that radiation therapy prolongs survival.[39] In addition, a few studies suggest that older women may be at decreased risk of local recurrence when compared with their younger counterparts.[19] Countering these arguments are the facts that, survival benefits aside, local recurrences may be difficult to manage (especially recurrences to skin), may require additional surgery or radiation therapy for local control, and may be psychologically devastating. Moreover, the apparent lower risk of recurrence may be an artifact of patient selection and of the extent of surgical excision.[19]

Similar arguments have been made for and against the use of axillary dissection in older women. Axillary dissection has been advocated as a therapeutic intervention because it eliminates residual disease and provides critical stage information. A recent report suggests that women ≥65 years of age who do not receive an axillary dissection have impaired survival compared with those who receive definitive therapy.[12] With respect to staging, the argument for not subjecting older women to axillary dissection is that a dissection is unnecessary if all older women are prescribed

tamoxifen and take it. Moreover, axillary dissection is associated with considerable morbidity.[40] Countering these arguments is the reality, observed clearly in the study reported herein, that not all older women, including high-risk women, receive adjuvant tamoxifen therapy. Furthermore, clinical evaluation of the axillary nodes has a false negative rate that ranges from 15% to 35%.[41] A potential alternative to axillary dissection is lymphatic mapping and sentinel node biopsy, but the technique may be less useful in older women because its success rate is lower in them.[42]

Although there is controversy regarding the effectiveness of radiation therapy and axillary dissection in older women, the evidence regarding adjuvant tamoxifen therapy is clearer. The 1998 St. Gallen 6th International Consensus Panel of the Treatment of Primary Breast Cancer recommended that with the exception of low-risk node negative patients (<10% risk of relapse at 10 years), all elderly patients should receive tamoxifen therapy except those who are estrogen receptor negative.[43] These recommendations are supported by the meta-analysis update of randomized trials that concluded that 5 years of tamoxifen therapy substantially reduces the risk of recurrence, mortality, and contralateral disease among women whose tumors are estrogen receptor positive. This benefit is independent of age, node status, and receipt of chemotherapy.[18] Although these latter findings were not available when the women studied herein were diagnosed, the 1990 NIH Consensus Conference stated that although "the majority of patients with node-negative breast cancer are cured by breast conservation treatment or total mastectomy and axillary dissection," combination chemotherapy or 2 years of tamoxifen is recommended.[44]

Our data, though limited, support the assertion that some high-risk patients may be undertreated, more often by male surgeons. Whether these treatment patterns will be reflected ultimately in variations in breast cancer–specific outcomes is not known. Outcome studies in this country have not included systemic adjuvant therapy, in part because both the Surveillance, Epidemiology, and End Results Program and local tumor registries do not collect such information, and because Medicare does not pay for tamoxifen. Addressing important questions about the effectiveness of primary tumor therapy and systemic adjuvant therapy will require longitudinal studies of large numbers of older women that collect detailed treatment information over follow-up periods of at least 5 years. Such studies are planned or in progress, but data will not be available for some time.

Meanwhile, our findings have implications for the care of older women with breast cancer. Surgeons provide the initial care, both diagnostic and therapeutic, for all women with breast cancer. Their discussions with women condition the broadening or narrowing of possible treatment options. Surgeons also facilitate referral to other breast cancer specialists: radiation and medical oncologists. Furthermore, they may be the ones who prescribe tamoxifen and monitor women for side effects and adherence, as well as for symptoms of recurrence. Thus, their role in breast cancer care is pivotal and has a substantial impact on the nature of breast cancer care received.

Our findings are consistent with those of others who have explored gender differences in primary care settings.[26,45] These studies have documented that female physicians are more nurturing and expressive and have a stronger interpersonal orientation than do their male counterparts. In interactions with their female patients, they contribute more equally to the interaction, allowing patients to tell their stories.[45] This aspect may be particularly important for the current generation of older women patients, who are less likely than younger women to be assertive and to ask questions. Regardless of whether or not this is a cohort effect, all women with newly diagnosed breast cancer will be better served by enhancing the quality of physician-patient communication. Thus, rather than recommending that more female surgeons should be trained or that older women with breast cancer should be referred to female surgeons for their care, we believe that greater emphasis needs to be placed on teaching effective communication skills to physicians. Although the development of interpersonal skills may come more easily to female physicians in general, all physicians will benefit from interviewing skills training during medical school, during postgraduate training, and beyond.[25] The methods for teaching these skills are well developed and have been shown to be effective.[47]

However, unless physicians have more time to talk with their patients and listen to them, such interventions are destined to fail. We need to think creatively about ways to help physicians provide information efficiently and effectively, whether by taking advantage of new technologies or by orga-

nizing some aspects of information sharing with groups of patients.[48] This is particularly important because of the increasing time pressures being placed on physicians who care for older patients, who often need more time to comfortably participate in their own health care decisions. Although future generations of older patients may be more assertive and facile with obtaining information from sources other than physicians, when faced with a potentially life-threatening disease such as breast cancer, they will still want their physicians to spend time with them and to discuss available options.

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Patient Characteristics and Treatments Associated with a Decline in Upper-body Function Following Breast Cancer Therapy

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ABSTRACT

Patient characteristics and treatments associated with a decline in upper-body function following breast cancer therapy

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Breast cancer therapy is often followed by a decline in upper-body function. 303 women diagnosed with Stage I or II breast cancer were interviewed 5 and 21 months after surgery and their medical records were reviewed. Women with cardiopulmonary comorbidity had an odds ratio for decline at the 5 month interview of 2.8 (95 percent CI 1.3-5.7), relative to women without. Women who received mastectomy (OR = 2.5; 95 percent CI 0.9-6.7) or breast conserving surgery with radiation therapy (OR = 2.9; 95 percent CI 1.0-8.9) were at higher risk for decline at the 5 month interview than women who received only breast conserving surgery. Women who had axillary dissection were more likely to report numbness or pain in the axilla (OR = 6.4; 95 percent CI 1.2-33) at the 21 month interview than women who did not. Clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with women who have early stage breast cancer.

Key Words: breast neoplasms, complications; breast neoplasms, therapy

Running title: Upper-body function decline following breast cancer

INTRODUCTION

Breast cancer is an important cause of morbidity and mortality among women. The American Cancer Society estimated that 178,700 women were diagnosed with breast cancer in 1998 and that 43,500 women died from the disease [1]. The large number of breast cancer cases diagnosed each year, in combination with the relatively favorable survival rates for treated patients, yields the largest group of cancer survivors in the U.S. population. Nearly two million living U.S. women have been diagnosed with breast cancer [2]. This sizeable pool of prevalent survivors suggests that the quality of life after breast cancer therapy is an important issue [3]. Quality of life strongly depends on physical function, both of which decline on average following breast cancer therapy [4].

While it is reasonable to expect that patients' upper-body function will decline following breast cancer therapy, studies have only recently characterized the nature, determinants, and duration of impairment [3-6]. An accurate understanding of the patient characteristics and therapy options that predispose towards upper-body dysfunction and discomfort is essential. Such an understanding would allow physicians to include consideration of the potential for these sequelae in their treatment recommendations and to prescribe exercise interventions that can be initiated before surgery.

This study assessed the effect of patient characteristics and therapy on self-reported upper-body function and discomfort 5 months after and 21 months after primary breast cancer therapy. The study provides some guidance as to the identification of patients likely to suffer upper-body sequelae and the treatments that may induce these adverse effects.

METHODS

Sampling

Details of the study have been described elsewhere [7]. An initial analysis of the effects of patient characteristics and therapy on upper-body function three to five months after definitive surgery has been presented [8]. The focus of the earlier presentation was to develop a parsimonious model to predict upper-body function decline. This presentation shows mutually adjusted effects of all patient characteristics and therapies, is not limited to a subset of respondents, and investigates effects at the first follow-up interview as well as at the baseline interview.

We studied women ≥ 55 years of age, newly diagnosed with histologically confirmed stage I or stage II invasive breast carcinoma, and treated at one of 5 hospitals in Boston, Massachusetts. We sent an introductory letter and a consent form to 388 potential study participants whose surgeons permitted contact. The letters were sent two to three months after the

patient's definitive surgical treatment. An interviewer followed-up with a telephone call to explain the study further, to answer questions, and to obtain informed consent. The average time from definitive surgery to baseline interview was 136 days (range 66 days to 293 days). We completed 90 percent of the baseline interviews by 185 days after definitive surgery. We attempted to contact all women for a follow-up interview. The average time from definitive surgery to the follow-up interview was 623 days, with a minimum of 473 days and a maximum of 1092 days. We completed 90 percent of the follow-up interviews by 693 days after definitive surgery.

Data collection

We reviewed patients' surgical records and conducted two 35-minute computer-assisted telephone interviews with consenting eligible patients. Data collected from medical records included: tumor size, axillary node status, breast surgery or surgeries performed (mastectomy or breast conserving surgery, with or without axillary dissection), side of surgery, and whether or not the patient received a course of post-operative radiation therapy.

Both the baseline and follow-up telephone interviews included three questions about tasks that required upper-body function: 1) pushing or pulling large objects, such as a living room chair, 2) lifting objects weighing more than 10 pounds, such

as a heavy bag of groceries, and 3) reaching or extending arms above shoulder level. We asked subjects to characterize the difficulty of each task as very difficult, somewhat difficult, or not difficult – or to say they did not do the task – during the four weeks preceding the interviews. We also asked subjects to characterize the difficulty of the tasks prior to their breast cancer treatment. We assumed that subjects who said they did not do a task had the most difficulty with that task, although we recognize that subjects might not do a task for reasons other than difficulty performing it. When we assumed that subjects who said they did not do a task had the least difficulty with that task, the results presented herein did not change substantially.

We selected these tasks to measure upper-body function from the items used by Satariano and colleagues [3], fielded previously in the Framingham Disability Study [9] and originally developed by Nagi [10].

We also asked subjects at the follow-up interview whether they were bothered by numbness or pain in their axilla as a result of surgery and whether they were bothered by swelling or problems with their arm as a result of surgery.

To characterize potential covariates, we asked questions about cardiopulmonary comorbidities that were part of the Total Illness Burden Index [11] and about patients' age, race, marital

status, education, number of people in the household, height, and weight.

Major analytic variables

Our primary dependent variable was a decline in upper-body function. Patients were classified as having an early decline in upper-body function for any task if they responded that any of the three tasks was more difficult at baseline interview than it was before breast cancer treatment. Patients were classified as having a late decline in upper-body function for any task if (1) they responded that any of the three tasks was more difficult at baseline interview than it was before breast cancer treatment and they did not recover to at least the baseline level of difficulty by the follow-up interview, or (2) they responded that any of the three tasks was more difficult at the follow-up interview than it was at the baseline interview.

Secondary dependent variables included two characterizations of upper-body discomfort. The first was a self-report at the follow-up interview of numbness or pain in the axilla as a result of surgery. The second was a self-report at the follow-up interview of swelling or problems with an arm as a result of surgery.

For our independent variables we considered: age (categories of 55-64, 65-74, 75+); education (< high school or ≥ high school); number of residents in the household (lives alone or

lives with somebody else); and marital status (married or other). We also considered body mass index (categorized as <25 kg/m^2, ≥25 to <30 kg/m^2, or ≥30 kg/m^2 [12]); tumor stage (stage I or stage II); side of surgery (categorized as right or both sides versus left side); breast cancer treatments received, cardiopulmonary comorbidity [13] (categorized as a score of 0, 1 to 3, or 4 or more – based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease or related symptoms of severity – with a higher score reflecting a diagnosis of at least one of the diseases or severe symptoms of the diseases without a formal diagnosis). A cardiopulmonary comorbidity score of 4 might reflect, for example, diagnoses of both heart attack and angina; or diagnosis of emphysema, chronic bronchitis or asthma; or diagnosis of congestive heart failure.

For the breast cancer treatments variables, we considered three primary treatments (breast conserving surgery followed by radiation therapy or simple mastectomy, versus receipt of breast conserving surgery with no radiation therapy) and whether or not subjects had axillary dissection.

Analytic Strategy

We performed a series of bivariate analyses, examining the relationships between independent variables and the dependent variables. Next, we developed a multiple logistic regression

model for each outcome: early decline in upper-body function, late decline in upper-body function, and each measure of upper-body discomfort. Because of the range of times between definitive surgery and the interviews, we included days between definitive surgery and the interviews in the applicable multivariable regression models. We did not perform survival analyses because the time to decline was determined by the date of interview, so does not correspond to the true time to the event.

RESULTS

We interviewed 303 women at the baseline interview following their definitive surgery. The 303 patients represent 78% of the 388 women whose surgeon permitted contact. Two hundred and fifty of the 303 women then completed the follow-up interview. Of the 53 women lost to follow-up, 5 died, 16 refused to participate in the follow-up interview, 2 were unable to participate because of poor health, and 30 could not be contacted. The women lost to follow-up were older, less likely to be married, and had lower body mass index, though these differences were not substantial. The risk of upper-body function decline did not depend on time to baseline or follow-up interview.

Table 1 shows the characteristics of the 303 women who completed the baseline interview. Of these women, 58% were ≥ 65 years of age. Most were white (93%) and had a high school

education or greater (83%). Half were married; most of the remainder were widowed. The average body mass index was 26.0 ± 0.3 kg/m^2 and the average comorbidity score was 1.5 ± 0.1. Most patients had small tumors (77% ≤ 2 cm) and were node negative (80%). The majority (65%) had undergone breast conserving surgery followed by radiation therapy; 24% had undergone mastectomy. Almost all (85%) had undergone axillary dissection.

At the baseline interview, 36% of subjects reported some decline in upper-body function and 7% reported a decline in all three of the upper-body function tasks. At the follow-up interview, 36% of subjects reported some decline in upper-body function and 4% reported a decline in all three of the upper-body function tasks. Two-thirds of the women who reported some decline in upper-body function at follow-up interview also reported a decline in upper-body function at the baseline interview.

The only patient characteristics associated with any early decline in upper-body function were cardiopulmonary comorbidity and education (see Table 2 for measures of the effect of patient characteristics on upper-body function decline). Women with a cardiopulmonary comorbidity score of 1, 2, or 3 had an odds ratio for any early upper-body function decline of 1.3 (95 percent CI 0.7-2.4), relative to women with a score of 0. Women with a cardiopulmonary comorbidity score of 4 or more had an odds ratio

for any early upper-body function decline of 2.8 (95 percent CI 1.3-5.7), relative to women with a score of 0. The latter association was attenuated for some late decline in upper-body function. Women with a cardiopulmonary comorbidity score of 1, 2, or 3 had an odds ratio for any late upper-body function decline of 1.2 (95 percent CI 0.6-2.4), relative to women with a score of 0. Women with a cardiopulmonary comorbidity score of 4 or more had an odds ratio for any late upper-body function decline of 1.7 (95 percent CI 0.8-3.8), relative to women with a score of 0. Women with at least a high school education were at lower risk for upper-body function decline at the 21 month interview (OR = 0.4; 95 percent CI 0.2-1.0).

Women who received mastectomy (OR = 2.5; 95 percent CI 0.9-6.7) or breast conserving surgery with radiation therapy (OR = 2.9; 95 percent CI 1.0-8.9) were at higher risk for upper-body function decline at the 5 month interview than women who received only breast conserving surgery.

At the follow-up interview, 37% of women reported numbness or pain in the axilla and 17% reported swelling or other problems with an arm. Older women were less likely than younger women to report numbness or pain in the axilla (see Table 3 for measures of the effect of patient characteristics on upper-body discomfort). In addition, women who lived alone were more likely

to have swelling or other arm problems than women who did not live alone (OR = 4.1; 95 percent CI 1.2-14).

Although the effect of axillary dissection on decline in upper-body function did not persist to the follow-up interview, axillary dissection did affect upper-body discomfort at the follow-up interview (see Table 3 for measures of the effect of patient characteristics on upper-body discomfort). Women who had axillary dissection were more likely to report numbness or pain in the axilla (OR = 6.4; 95 percent CI 1.2-33) than women who did not have axillary dissection.

DISCUSSION

As reported previously [8], breast cancer patients with cardiopulmonary comorbidity or who received definitive primary therapy (breast conserving surgery and radiation therapy, or mastectomy) are at increased risk of decline in upper-body function during the five months following primary breast cancer therapy. Age, marital status, living alone, and side of surgery were not related to decline in upper-body function in either the 5 months following definitive surgery or at the 21-month follow-up.

Axillary dissection was an important cause of upper-body discomfort at the follow-up interview 21 months after definitive surgery. Approximately 40% of women who had axillary dissection reported pain in their axilla at the follow-up interview,

compared to 7% of those who did not have axillary dissection. Approximately 20% of women who had axillary dissection reported swelling or other arm problems at the follow-up interview, compared to 3% of women who did not have axillary dissection. Younger women were more likely than older women to report upper-body discomfort and women who lived alone were more likely to report swelling or other arm problems than women who did not live alone. Marital status, education, side of surgery, and cardiopulmonary comorbidity were not related to upper-body discomfort at the follow-up interview.

Axillary node dissection may increase the risk of decline in upper-body function in the 5 months after treatment, but not the risk of persistent decline or delayed onset of decline 21 months after definitive surgery. As expected, axillary dissection appears to increase the risk of numbness or pain in the axilla, even two years after diagnosis.

Our findings are consistent with previous investigations of upper-body function after treatment for early stage breast cancer. Liljegren and colleagues found that older patients and patients who underwent less extensive axillary dissection were at lower risk for arm symptoms at both 3-12 months and 13-36 months after treatment [14]. Three other investigations also found that the prevalence of upper-body sequelae depended on the extent of axillary dissection [15, 16, 17]. Ganz and colleagues found that

measures of quality life after treatment did not depend on receipt of breast conserving surgery versus modified radical mastectomy, except that patients who received the latter primary therapy were more likely to report problems with clothing and body image [18]. Tasmuth and colleagues found that the occurrence of arm sequelae did not depend on whether the patient received breast conserving surgery or modified radical mastectomy and that reaching out, carrying heavy objects, working with the ipsilateral arm, and housework aggravated the arm symptoms [19]. These aggravating factors may be among the influences captured in our finding that women who live alone were more likely to report swelling or other arm problems.

Gerber and colleagues found that women who received modified radical mastectomy recovered their pre-operative range of motion more slowly than women who received local excision and radiation therapy [5]. The difference in recovery time for functional range of motion was not as large as the difference in recovery time for pre-operative range of motion. Sneeuw and colleagues examined functional outcomes four years after treatment among women who received breast conserving surgery, axillary dissection, and radiation therapy [6]. Nearly half of the subjects reported a little (34%) or moderate (13%) limitation of movement in the arm and shoulder on the treatment side.

Axillary node dissection is an important prognostic indicator for women with early stage breast cancer [20]. Removal of level 1 and level 2 nodes is currently recommended for accurate staging and to reduce the risk of recurrence in the axilla, unless the risk of axillary metastasis is very low or when knowledge of node status will have no influence on therapy [21]. Reliable indicators of node status to stage disease accurately when no axillary dissection is performed, however, have been difficult to identify [22].

Although there is a general consensus regarding the current need for axillary dissection to facilitate staging and to avoid axillary metastasis, the extent of dissection remains controversial [21]. Axillary sampling of 3 to 5 nodes, which had shown some promise [23], has largely been abandoned in favor of dissection of only level I and level II nodes [21, 24, 25]. Levels I and II dissection yields 10 or more nodes, which is usually sufficient to determine the breast cancer stage [21]. The advent of lymphatic mapping and sentinel lymph node biopsy may further reduce the extent of recommended axillary dissection [26]. In three recent series of clinically node-negative breast cancer patients, sentinel lymph node biopsy detected between 89% and 98% of patients with positive nodes by level I-III axillary dissection and all patients with negative nodes by level I-III axillary dissection had a negative sentinel lymph node biopsy

[27, 28, 29]. While these results suggest that sentinel node biopsy may eventually supplant axillary dissection for breast cancer staging, current recommendations conclude that it would be premature to abandon axillary dissection in favor of sentinel node biopsy [30] without clinical trials to establish its safety and efficacy [31]. Furthermore, axillary dissection will remain an important component of prognostic evaluation for women whose sentinel node biopsy results are positive.

Our findings must be considered with the study's major limitations in mind. First, we did not directly measure upper-body function, either before or after treatment. We asked women to recall their upper-body function prior to their treatment, and then compared their current self-reported function to the prediagnosis function as a measure of upper-body function decline. While this method may misclassify decline in upper-body function, we do not expect the misclassification to depend on cardiopulmonary comorbidity status or primary therapy. Non-differential misclassification of upper-body function would bias the estimated effect of cardiopulmonary comorbidity towards the null on average. Differential recall is more likely associated with axillary dissection, a surgical intervention that women may expect will cause a decline in upper-body function. We would not, however, expect this differential recall to dissipate by the 21-month time point, and axillary dissection was only associated

with upper-body function decline between the prediagnosis assessment and the 5 month time point. In addition, the score of self-reported prediagnosis upper-body function summed over the three tasks did not depend on any of the patient or therapy characteristics (2-sided null p-value for the association with breast conserving surgery and radiation therapy = 0.79, with mastectomy = 0.76, and with axillary dissection = 0.82) except the cardiopulmonary comorbidity index (2-sided null p-value = 0.0004), which reflects the impact of diseases that existed at the time of the first interview. These findings suggest that the self-reported assessment of prediagnosis upper-body function was not biased by the therapy that the participants received. We conclude that differential misclassification is unlikely to account for the entire association between cardiopulmonary comorbidity, primary therapy, or axillary dissection, and upper-body function decline.

Furthermore, some earlier investigators have argued that patient's self-report of arm function is likely to be more relevant than objective measures [32, 33, 34]. These investigators contend that objective measures of function do not adequately reflect patients' perceptions of their function and ability to perform activities of daily living. Patients with poor objective measures may report no impact on their upper-body

function and patients with poor self-reported function may score in the normal range of objective measures.

Second, we did not gather side of surgery information in relation to handedness. One earlier investigation showed that grip strength declined more if surgery was performed on the side of the dominant hand [19]. As a crude approximation, we measured the effect of side of surgery on the upper-body outcomes. If one assumes that all women in the cohort are right handed, then side of surgery crudely approximates the effect of surgery on the side of a woman's dominant hand. Approximately 6% of women in the study's age range are expected to be left handed [35], so would be misclassified as right handed in this analysis. Side of surgery had no effect on upper-body function decline or discomfort. If surgery on the side of the dominant hand is more likely to result in upper-body function decline than surgery on the side of the less dominant hand, we would have expected to see some effect. It may be that the measures of upper-body function decline are too crude to detect a hand-dependent effect. Measures of fine motor control or sensation, for example, may be more dependent on whether surgery occurs on the side of the dominant hand.

Third, we did not collect information about prior recreational or occupational injuries involving the upper extremities. We do not expect these to depend on the variables

included in the analysis, so the reported measures of effect should not be confounded by these prior conditions.

Fourth, we did not measure upper-body function decline in a control population that was not diagnosed with breast cancer. Thus, we cannot measure the effect of the diagnosis and/or receipt of any primary therapy on upper-body function and discomfort. Satariano and Ragland [36] measured the prevalence of upper-body function limitation in both a control population and a population of breast cancer patients. They defined a limitation as any report of a lot of difficulty, or that the task was not performed on doctor's orders, for any of the upper-body tasks originally developed by Nagi [10]. Using a similar definition for upper-body limitation at baseline interview, and stratifying our population into the age groups used by Satariano and Ragland [36], we found that the prevalence of upper-body limitation in our population of breast cancer patients more closely resembled the prevalence of upper-body limitation in the control population of Satariano and Ragland [36] than the prevalence in their population of breast cancer patients (data not shown). Satariano and Ragland asked subjects about limitations in lifting items that weigh less than ten pounds, and we did not. The difference in prevalence of upper-body limitation between our breast cancer patients and their breast

cancer patients may be partly explained by their inquiry about this additional task.

Given the critical importance of upper-body function in maintaining independent living [37], our findings suggest that clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with older women who have early stage breast cancer. Strategies to prevent overcompensation for discomfort or weakness on the side of surgery by overusing the opposite side should also be outlined.

This study demonstrates that upper-body dysfunction can arise shortly after therapy and resolve, arise and persist for at least 21 months, or arise at some time distant from therapy. Therefore, the upper-body function of all breast cancer patients should be followed and appropriate interventions planned for at least two years after diagnosis. In time, surgeons and patients may be able to substitute sentinel node biopsy for axillary dissection to reduce the impact of breast cancer therapy on upper body function.

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Table 1. Characteristics of the cohort

Characteristic	Number	Percent
Age group		
55-64 years	126	42%
65-74 years	111	37%
75+ years	66	22%
Race		
White	281	93%
African American	13	4%
Hispanic	2	0.7%
Asian or Pacific Islander	3	1%
Other	2	0.7%
Missing	2	
Education		
< High School	51	17%
≥ High School	249	83%
Missing	3	
Number in House		
Lives with someone	197	66%
Lives alone	103	34%
Missing	3	

Characteristic	Number	Percent
Marital Status		
Other than married	153	51%
Married	148	49%
Missing	7	
Body Mass Index		
<25 kg/m2	143	48%
≥25 to <30 kg/m2	100	34%
≥30 kg/m2	55	19%
Missing	5	
Tumor Stage		
Stage 1	193	64%
Stage 2	109	36%
Missing	1	
Side of Surgery		
Left Only	123	49%
Right or Both	126	51%
Missing	54	

Characteristic	Number	Percent
Cardiopulmonary Comorbidity Score		
Zero	180	59%
One, two or three	73	24%
Four to fifteen	50	17%
Primary therapy		
Mastectomy	71	23%
Breast conserving surgery and radiation therapy	195	64%
Breast conserving surgery and no radiation therapy	33	11%
Other	4	1%
Axillary Dissection		
No	44	15%
Yes	258	85%
Missing	1	

Table 2. Effect of patient characteristics and therapy on early and late upper-body function

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Age group						
55-64 years	45/126	36%	1.	36/107	34%	1.
65-74 years	40/110	36%	0.9 (0.5-1.7)	32/95	34%	0.8 (0.4-1.5)
75+ years	21/62	34%	1.2 (0.5-2.7)	23/48	48%	1.1 (0.4-2.6)
Missing	5			7		

	Decline from baseline to 5 month interview		Decline from baseline to 21 month interview	
	# declining/ total % Declining	adjusted* OR (95% CI)	# declining/ total % Declining	adjusted* OR (95% CI)
Race†				
White	100/276	36%	84/237	35%
African American	5/13	38%	4/9	44%
Hispanic	1/2	50%	1/1	100%
Asian or Pacific Islander	0/2	0%	1/2	50%
Other	0/2	0%		
Missing	7		2	

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Education						
< High School	30/50	40%	1.	22/40	55%	1.
≥ High School	86/246	35%	0.9 (0.4-1.7)	68/209	33%	0.4 (0.2-1.0)
Missing	7			2		
Number in House						
Lives with someone	67/194	35%	1.	50/164	30%	1.
Lives alone	38/101	38%	1.0 (0.5-2.2)	39/84	46%	1.5 (0.7-3.5)
Missing	8			3		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total % Declining		adjusted* OR (95% CI)	# declining/ total % Declining		adjusted* OR (95% CI)
Marital Status						
Other than married	58/148	39%	1.	55/121	45%	1.
Married	48/148	32%	0.8 (0.4-1.6)	35/128	35%	0.7 (0.3-1.6)
Missing	7			2		
Body Mass Index						
<25 kg/m2	46/141	33%	1.	44/116	38%	1.
≥25 to <30 kg/m2	34/99	34%	1.0 (0.6-1.8)	26/84	31%	0.6 (0.3-1.3)
≥30 kg/m2	26/55	47%	1.5 (0.7-3.1)	20/48	42%	1.0 (0.5-2.3)
Missing	8			3		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Tumor Stage						
Stage 1	65/188	35%	1.	61/163	37%	1.
Stage 2	41/109	38%	1.0 (0.5-1.7)	30/87	34%	0.9 (0.5-1.7)
Missing	6			1		
Side of Surgery†						
Left Only	42/123	34%	1.	45/120	38%	1.
Right or Both	46/125	37%	1.2 (0.7-2.0)	41/124	33%	0.8 (0.5-1.4)
Missing	55			7		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total % Declining		adjusted* OR (95% CI)	# declining/ total % Declining		adjusted* OR (95% CI)
Cardiopulmonary						
Comorbidity Score						
Zero	53/177	30%	1.	46/145	68%	1.
One, two or three	27/72	38%	1.3 (0.7-2.4)	23/62	63%	1.2 (0.6-2.4)
Four to fifteen	26/49	53%	2.8 (1.3-5.7)	22/43	49%	1.7 (0.8-3.8)
Missing	5			1		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Primary therapy						
Mastectomy	30/69	43%	2.5 (0.9-6.7)	21/55	38%	1.3 (0.5-3.6)
Breast conserving surgery and radiation therapy	69/194	36%	2.9 (1.0-8.9)	59/168	35%	1.3 (0.4-4.3)
Breast conserving surgery and no radiation therapy	6/31	20%	1.	11/27	41%	1.
Other	9			1		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Axillary Dissection						
No	10/40	25%	1.	15/30	50%	1.
Yes	95/257	95/2	2.5 (0.9-6.6)	75/219	34%	0.8 (0.3-2.2)
Missing	6	57		2		

*Unless otherwise indicated, adjusted for the effects of the other listed variables, time to baseline interview, and time to follow-up interview (for dependent variables measured at the follow-up).

†Race was not included in the multivariable models because of the small number of nonwhite subjects.

‡The effect of side of surgery was adjusted for the other variables. Side of surgery was not included in the multivariable models to estimate the effects of the other variables because of the high proportion of subjects for whom side of surgery was unknown.

Table 3. Effect of patient characteristics on numbness, pain or swelling at follow-up interview

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Age group						
55-64 years	60/105	57%	1.	19/105	18%	1.
65-74 years	26/93	28%	0.2 (0.1-0.5)	19/94	20%	1.2 (0.5-2.7)
75+ years	6/48	13%	0.1 (0.03-0.3)	4/48	8%	0.3 (0.1-1.3)
Missing	5			4		

	Numbness or pain in the axilla		Swelling in the arm	
	# declining/ total % Declining	adjusted* OR (95% CI)	# declining/ total % Declining	adjusted* OR (95% CI)
Race†				
White	85/234 36%		39/235 17%	
African American	5/8 63%		2/8 25%	
Hispanic	0/1 0%		0/1 0%	
Asian or Pacific Islander	1/2 50%		1/2 50%	
Other	7			
Missing			5	

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Education						
< High School	14/40	35%	1.	8/40	20%	1.
≥ High School	77/205	38%	0.5 (0.2-1.2)	34/206	17%	0.8 (0.3-2.2)
Missing	7			5		
Number in House						
Lives with someone	65/161	40%	1.	25/162	15%	1.
Lives alone	26/83	31%	1.5 (0.6-3.6)	17/83	20%	4.1 (1.2-14)
Missing	8			6		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total % Declining		adjusted* OR (95% CI)	# declining/ total % Declining		adjusted* OR (95% CI)
Marital Status						
Other than married	39/119	33%	1.	20/119	17%	1.
Married	52/126	41%	1.2 (0.5-2.7)	22/127	17%	2.3 (0.7-7.1)
Missing	7			5		
Body Mass Index						
< 25 kg/m2	43/113	38%	1.	15/114	13%	1.
≥25 to <30 kg/m2	27/83	33%	0.6 (0.3-1.3)	14/83	17%	1.0 (0.4-2.5)
≥30 kg/m2	21/48	44%	0.7 (0.3-1.6)	13/48	27%	2.4 (0.9-6.7)
Missing	8			6		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Tumor Stage						
Stage 1	58/160	36%	1.	21/161	13%	1.
Stage 2	34/86	40%	0.9 (0.5-1.7)	21/86	24%	2.0 (0.9-4.3)
Missing	6			4		
Side of Surgery						
Left Only	45/119	38%	1.	24/120	20%	1.
Right or Both	46/125	37%	1.1 (0.6-1.9)	18/125	14%	0.6 (0.3-1.2)
Missing	8			6		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total % Declining		adjusted* OR (95% CI)	# declining/ total % Declining		adjusted* OR (95% CI)
Cardiopulmonary Comorbidity Score						
Zero	54/142	38%	1.	26/143	18%	1.
One, two or three	22/61	36%	1.3 (0.6-2.8)	10/61	16%	0.7 (0.3-1.7)
Four to fifteen	16/43	37%	1.9 (0.8-4.5)	6/43	14%	0.6 (0.3-1.7)
Missing	3			4		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Primary therapy						
Mastectomy	19/53	36%	1.6 (0.4-6.2)	13/53	25%	2.5 (0.5-13)
Breast conserving surgery and radiation therapy	66/166	40%	2.2 (0.6-7.5)	26/167	16%	1.5 (0.3-7.0)
Breast conserving surgery and no radiation therapy	5/25	20%	1.	3/25	11%	1.
Other	4			4		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Axillary Dissection						
No	2/30	7%	1.	1/30	3%	1.
Yes	90/216	42%	6.4 (1.2-33)	41/217	19%	3.8 (0.4-34)
Missing	6			4		

*Unless otherwise indicated, adjusted for the effects of the other listed variables and time to follow-up interview.

†Race was not included in the multivariable models because of the small number of nonwhite subjects.

Adjuvant Tamoxifen: Predictors of Use, Side Effects, and Discontinuation in Older Women

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Running Head: Adjuvant Tamoxifen in Older Women

Abstract

PURPOSE: To identify predictors of adjuvant tamoxifen use, side effects, and discontinuation in older women.

METHODS: We followed a cohort of 303 women 55 years of age or older diagnosed with stage I or stage II breast cancer for nearly three years following primary tumor therapy. Data were collected from women's surgical records and from computer-assisted telephone interviews at 5, 21, and 33 months following primary tumor therapy.

RESULTS: Two hundred and ninety-two of the 303 (96%) patients in the study provided information about tamoxifen use. Tamoxifen use was reported by 189 (65%) patients; 26 (15%) discontinued use during the follow-up period. Being older (65-74 vs. 55-64 years of age), having stage II disease, being estrogen receptor positive, seeing a greater number of breast cancer physicians, and having better perceptions of one's abilities to discuss treatment options with physicians were associated with a greater odds of tamoxifen use. Better physical function, having received standard primary tumor therapy, and having obtained helpful breast cancer information from books or magazines were associated with lesser odds of tamoxifen use. The oldest patients (75+ years) [relative to youngest old (55-64 years)] and patients with better emotional health had significantly lesser odds of reporting side effects. Patients who were estrogen receptor positive were less likely to stop taking tamoxifen; patients who experienced side effects were more likely to stop taking tamoxifen.

CONCLUSIONS: Deviations from a prescribed course of adjuvant tamoxifen occur relatively frequently. The clinical consequences of this deviation need to be identified and quantified.

Adjuvant Tamoxifen: Predictors of Use, Side Effects, and Discontinuation in Older Women

Introduction

An estimated 178,700 women were diagnosed with breast cancer in 1998 (1), more than half of whom were 65 years of age or older (2). A substantial literature has documented that older women are less likely to receive standard care for a new diagnosis of breast cancer (3-14). Although less than standard therapy has been linked to higher rates of breast cancer recurrence and mortality (15-18), it is not known whether this is due to deficiencies in primary tumor therapy, deficiencies in the prescribing of and adherence to systemic adjuvant therapy, or both.

Over the past decade, the threshold for recommending systemic adjuvant therapy has progressively lowered and the focus has shifted from reducing mortality to improving recurrence-free survival (19). For example, the 1990 NIH Consensus Development Conference on the treatment of early stage breast cancer noted that while "the majority of patients with node-negative breast cancer are cured by breast conservation treatment or total mastectomy and axillary dissection," combination chemotherapy or at least two years of tamoxifen was recommended (20). By early 1998, systemic adjuvant therapy was recommended for all women except for those node negative women at low risk of recurrence by virtue of having tumors 1 cm or less in diameter or having grade 1, estrogen receptor positive tumors with no lymphatic invasion (21, 22). Tamoxifen was recommended also for node negative women over 70 years of age at high risk of recurrence, regardless of estrogen receptor status (22). The 1998 St. Gallen 6th International Consensus Panel on the Treatment of Primary Breast Cancer further refined

these guidelines (23). With the exception of low risk node negative patients (less than a 10% risk of relapse at 10 years) and those who are estrogen receptor negative, the Panel recommended a full five years of tamoxifen therapy for all elderly women with breast cancer (23). These recommendations were undoubtedly influenced by the overview update of randomized trials of adjuvant tamoxifen therapy that concluded that five years of tamoxifen therapy substantially reduces the risk of recurrence, mortality, and contralateral disease among women whose tumors are estrogen receptor positive and that this benefit is independent of age, node status, and receipt of chemotherapy (24).

Although five years of adjuvant tamoxifen therapy is now recommended (22, 23), information about tamoxifen adherence and discontinuance rates is sparse. We know of no published data regarding tamoxifen discontinuance rates in clinical practice. In the context of clinical trials, discontinuance rates have ranged from 23% to 40%. In the tamoxifen chemoprevention trials for example, the Royal Marsden Hospital trial reported a 40% premature discontinuance rate in the treatment group during a median follow-up of 70 months (5.8 years), compared to 31% of women in the placebo group (25). The NSABP Breast Cancer Prevention Trial reported that 24% of women in the tamoxifen group discontinued therapy, compared to 20% of women in the placebo group (26). In the adjuvant tamoxifen setting, Fisher and colleagues reported that 23% of patients participating in the B-14 trial discontinued tamoxifen therapy prior to the occurrence of an event during the first five years following randomization, compared to 24% of women in the placebo group (27).

To better understand patterns of adjuvant tamoxifen use and discontinuation, we followed a cohort of 303 women 55 years of age or older who were diagnosed with stage

I or stage II breast cancer for nearly three years following primary tumor therapy. Specifically, we sought to identify predictors of adjuvant tamoxifen use, side effects, and discontinuation.

Methods

Study Sample

The study's methods have been described (14). To be eligible for study participation, women had to be 55 years of age or older, newly diagnosed with stage I or stage II breast cancer, and have no history of a prior breast cancer. Eligible women were sent an introductory letter and a consent form following their most definitive surgical treatment. Our interviewer followed-up by telephone and provided additional information about the study, answered questions, and obtained informed consent. Subjects were enrolled between January 1993 and April 1996.

Data Collection

Data were collected from women's surgical records and from computer-assisted telephone interviews at 5, 21, and 33 months following primary tumor therapy. Data collected from medical records included: histology, stage, estrogen receptor status, and surgeries performed (modified radical mastectomy or breast conserving surgery). Medical records were monitored for six months following surgery to determine whether radiation therapy and chemotherapy were initiated and completed, and whether adjuvant tamoxifen therapy was initiated. The baseline telephone interview included questions about sociodemographic characteristics (including age, education, and marital status); general health-related quality of life (as measured by the Medical Outcomes Study Short Form (SF-36) (28); breast cancer-specific quality of life, the presence of physician-

diagnosed cardiopulmonary diseases and the frequency of associated symptoms; the number of physicians with whom breast cancer treatment options were discussed and the specific treatments chosen; the perceived helpfulness of various sources of information about breast cancer and its treatment; and perceptions of doctor-patient communication. Follow-up interviews asked detailed questions about adjuvant tamoxifen use, side effects, and discontinuance.

Major Analytic Variables

Outcome variables

Tamoxifen use was defined as taking tamoxifen at any time during the study period (from baseline through the second follow-up interview). At each interview patients were asked, "Are you taking tamoxifen at the present time?" At the second follow-up interview they were also asked, "Did you ever take tamoxifen?" when the answer to the first tamoxifen use question was "no." Responses across the three interviews were then summarized as a dichotomous variable with a "yes" or "no" response to ever having taken tamoxifen.

Side effects: Information on side effects was collected only from those patients who reported taking tamoxifen. Patients were asked if they were experiencing hot flashes, vaginitis, phlebitis, depression, nausea, edema, or any other side effects. Two dichotomous side effect variables with yes/no responses were considered for analysis: hot flashes alone and any side effects. The definition of the latter variable included hot flashes as well as reports of any other side effects. We chose to consider both definitions because we expected the reporting of hot flashes to be highly age dependent but the reporting of any side effects to be less so.

Discontinuation of tamoxifen therapy: Whether or not women were continuing to take tamoxifen was evaluated at the second follow-up interview. For patients with missing tamoxifen information we employed the last observation carried forward (LOCF) approach to fill in the missing values (29). We categorized women as either still taking tamoxifen ("yes") or no longer taking tamoxifen ("no"). Patients who had experienced a breast cancer recurrence by the second follow-up interview were excluded from this definition.

Explanatory variables

We considered variables from five categories. First, we considered sociodemographic characteristics, including age (55-64, 65-74, and 75+ years), marital status (currently married/not married), and education (< high school/≥ high school). Second, we considered two measures of health status: comorbidity and physical function. Our measure of comorbidity was based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease, as well as related disease manifestations (30). We evaluated physical function using the 10-item physical function scale from the SF-36 (28). Third, we considered two measures of emotional health: 1) the 5-item measure of general emotional health from the SF-36 (28), and 2) a 4-item measure of breast cancer-specific emotional health that assesses feelings and worries due to potential problems related to the progression of breast cancer (31). Fourth, we considered breast cancer related variables: breast cancer stage (I/II), estrogen receptor status (positive/negative), and whether patients received standard primary tumor therapy, defined as modified radical mastectomy or breast conserving surgery and axillary dissection followed by radiation therapy (yes/no). Fifth, we considered aspects

of the treatment decision-making process: 1) sources of helpful information about breast cancer and its treatment; 2) the number of breast cancer specialists with whom the patient discussed treatment options; 3) patients' perceptions of their abilities to communicate with their physicians; 4) patients' perceptions of their physicians' abilities to give information, discuss treatment options, and tailor treatments; and 5) patients' rating of their physicians' technical and interpersonal care (31).

Data Analysis:

To explore the crude associations between categorical and continuous variables we used two-sample t-tests (or analysis of variance procedure, ANOVA) and for associations between categorical variables we used chi-square tests of proportions (or Fisher's Exact-test when needed). The association between each of the three outcome variables and the explanatory variables was evaluated using multiple logistic regression analysis. In this multivariable analysis, all of the explanatory variables were eligible to enter the final model. We used a stepwise selection procedure to develop parsimonious models. Due to variations in tamoxifen use by estrogen receptor status, we also performed separate analyses for estrogen receptor positive patients. There was insufficient information to perform subgroup analyses for patients who were estrogen receptor negative. Results with p-values less than 0.05 were deemed to be statistically significant in this report.

Results

Sample characteristics: The average age of patients was 67.7 (SD=8.7) years. About half were married and 83% had completed at least a high school education. Fifty-nine percent had no cardiopulmonary comorbidity, 63% had stage I breast cancer, the

majority (76%) were estrogen receptor positive, and 78% had received definitive primary tumor therapy. Two hundred and ninety-two of the 303 (96%) patients in the study provided information about tamoxifen use. Tamoxifen use was reported by 189 (65%) patients. Among patients who took tamoxifen, 166 (88%) provided information about their experience of side effects. One hundred four (63%) reported at least one side effect while they were taking tamoxifen: hot flashes (45%), vaginitis (16%), fluid retention (13%), depression (15%), nausea (7%), fatigue (5%), thrombophlebitis (2%), vision problems (2%), vaginal bleeding (2%), and other side effects (17%). Twenty-six patients (15%) had stopped taking tamoxifen by the time of second follow-up interview for reasons other than recurrence of breast cancer. Of these, 18 (69%) were estrogen receptor positive and 8 (31%) were estrogen receptor negative. Thirteen patients had breast cancer recurrence and were excluded from the adherence analysis because we were uncertain whether they had stopped taking tamoxifen before or after their recurrences were clinically apparent.

Summary information regarding our explanatory variables by patient age is displayed in Table 1. Younger patients were more likely to be married and were more highly educated. As expected, they were less likely to have comorbidity and their physical function scores were higher. Emotional health status did not vary by age. Younger patients were more likely to have received definitive primary tumor therapy. They were more likely to report that they obtained helpful breast cancer information from books or magazines and television spots; they saw a greater number of breast cancer physicians; they rated their and their physicians' abilities to communicate more highly; and they rated their physicians' technical and interpersonal skills more highly.

Tamoxifen use: Table 2 displays the results of our multiple logistic regression analysis with tamoxifen use as the outcome. Older age (65-74 vs. 55-64 years of age), having stage II disease, and being estrogen receptor positive were associated with a statistically significantly greater odds of tamoxifen use. In addition, seeing a greater number of breast cancer physicians and having better perceptions of one's abilities to discuss treatment options with physicians were statistically significantly associated with greater odds of tamoxifen use. In contrast, better physical function, having received standard primary tumor therapy, and having obtained helpful breast cancer information from books or magazines were associated with lesser odds of tamoxifen use.

Findings from a logistic regression analysis based on the subset of patients who were estrogen receptor positive were similar to the findings from the full data set for all explanatory variables except for age. Among estrogen receptor positive patients, there were no statistically significant differences in the odds of tamoxifen use among the three age groups.

Side effects: The multiple logistic regression analysis with any side effects as the outcome (Table 3, Model A) indicates that the oldest old patients (75+ years) [relative to youngest old (55-64 years)] and patients with better emotional health had significantly lesser odds of reporting side effects. Findings were similar when the outcome was restricted to hot flashes (Table 3, Model B). In addition, educational attainment was associated with reporting hot flashes. Patients who completed at least the 12^{th} grade were over five times more likely to report hot flashes than those who did not complete high school education.

Tamoxifen Discontinuation: Patients who were estrogen receptor positive were less likely to stop taking tamoxifen during the follow-up period and patients who experienced side effects were more likely to stop taking tamoxifen (Table 4). Age and standard primary tumor therapy were not statistically significantly associated with tamoxifen discontinuance. Although the relationship between standard primary tumor therapy and tamoxifen discontinuance was not statistically significant, the data suggest that patients who received standard primary tumor therapy were less likely to stop taking tamoxifen. This relationship was similar for the subset of patients who were estrogen receptor positive and the full data set.

Discussion

In this study of older women with early stage breast cancer, we have found that, in addition to clinical factors, age, physical function, standard primary tumor therapy, and aspects of the decision-making process were associated with tamoxifen use. The associations between older age, poorer physical function, and less than standard primary tumor therapy and tamoxifen use suggest the substitution of tamoxifen for therapies with greater likelihood of side effects and its use in women with poorer physical capacity. It is of interest, however, that while women 65-74 years of age were more likely than women 55-64 years of age to take tamoxifen, this was not true for the oldest women (75+ years of age). This oldest group was about as likely to take tamoxifen as was the youngest group.

As we have found in studies of primary tumor therapy (14) and of the combination of primary tumor therapy and systemic adjuvant therapy (32), aspects of doctor-patient communication are independently associated with tamoxifen use. In the

case of tamoxifen, the number of breast cancer specialists seen and patients' confidence in their abilities to communicate with their physicians about breast cancer-related issues were both independently associated with its use. The diagnosis of breast cancer is frightening and it may take several conversations with physicians for women to truly understand their options.

With respect to side effects, the oldest women and those with better emotional health at baseline were less likely to report experiencing side effects. This was also true when the analysis was restricted to hot flashes. The fact that the oldest women were less likely to report side effects is consistent with the fact that these women have the lowest levels of circulating estrogen and are therefore least likely to be affected by the anti-estrogenic effects of tamoxifen. In addition, older persons in general are more likely to tolerate cancer treatments than are their younger counterparts (33). Women whose baseline general emotional health scores were lower (worse) were more likely to report side effects. Again, this is consistent with what is well-described in persons with mood disorders. Somatic symptoms are more likely to be reported by older (60+ years) community dwelling persons with major depression as well as dysthymia than by their healthy counterparts (34).

Women who were estrogen receptor negative and those who reported side effects were more likely to have stopped taking tamoxifen by three years after diagnosis. The former is not surprising, given the recent data suggesting that tamoxifen is less beneficial in women with estrogen receptor negative tumors (23), and the latter could be anticipated. The individual side effects significantly associated with stopping tamoxifen were depression, nausea, visual complaints, and vaginal bleeding. It is potentially of

concern that, although not statistically significant, those women who received less than definitive primary tumor therapy, a setting in which we found tamoxifen to be used preferentially, were more likely to have stopped taking tamoxifen by three years after diagnosis. This is particularly true since women who were at low risk of recurrence by virtue of having very small tumors were not more likely to stop taking tamoxifen than those at moderate or high risk. The substitution of tamoxifen for elements of standard primary tumor therapy may, in the longer term, put these women at higher risk of recurrence and breast cancer mortality if they are more likely to stop taking it prematurely.

Although our findings represent some of the first to examine tamoxifen use and its sequelae among older women with early stage breast cancer cared for in the community, they must be accepted with the following caveats. First, other than at baseline, we did not collect tamoxifen use information from medical records. Although we think that it is unlikely that women would report that they had stopped taking tamoxifen when in fact they had not, it is possible that women who reported continuing to take it had indeed stopped taking it. Were this the case, we would have underestimated the number of women who had discontinued tamoxifen therapy. Second, our sample of older women was relatively young, well-educated, and in good health. Variations in tamoxifen prescribing, side effects, and discontinuance might have been greater had our sample been more heterogeneous. Third, losses to follow-up and our reliance on annual telephone interviews precluded the collection of detailed temporal information about tamoxifen discontinuance. However, our strategy of excluding from analysis the 13 women who experienced recurrences should have minimized the impact of this

circumstance. Fourth, we studied patterns of tamoxifen use during a period of time when guidelines for use were changing. Fifth, our sample is too small and our follow-up has not been long enough to ascertain whether the variations in primary tumor therapy and adjuvant tamoxifen therapy observed will be reflected in variations in the critically important outcomes of breast cancer recurrence and breast cancer-specific mortality. Larger and longer term studies are needed to examine these questions, since it is unlikely that clinical trials of therapies known to be efficacious in younger postmenopausal women will be undertaken to confirm or disprove their efficacy in older postmenopausal women. Furthermore, with broader indications for adjuvant tamoxifen and longer durations of recommended therapy, it is critical that patterns of discontinuance and their consequences be identified and quantified. While the 15% discontinuation rate that we observed appears favorable in comparison to that observed in the NSABP B-14 trial (23%), it still represents a significant degree of discontinuation and is perhaps greater than might be appreciated by many practicing oncologists.

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Table 1. Study Variables by Age Group

	55-64 (N=125) n (%)	65-74 (N=108) n (%)	75 + N=59 N (%)	*P-value*
Sociodemographics				
Marital Status				
Married	73 (59)	57 (53)	14 (24)	<0.01
Education				
≥ High School	111 (90)	89 (82)	41 (70)	<0.01
Health Status				
Comorbidity				
None	86 (69)	58 (54)	29 (49)	0.03
Physical Function	79.2	74	60.6	<0.01
Emotional Health				
General	72.2	75.5	74.8	0.35
Breast Cancer-specific	65.1	66.7	65.7	0.83
Breast Cancer – related				
Stage I	73 (59)	71 (66)	40 (68)	0.40
Estrogen Receptor Positive	81 (73)	78 (75)	45 (87)	0.15
Standard Primary Therapy	112 (90)	90 (83)	27 (46)	<0.01
Treatment Decision-making				
Sources of Information				
Books/Magazines	74 (59)	48 (45)	10 (18)	<0.01
Television Spots	26 (21)	21 (20)	1 (2)	<0.01
Number of Physicians Seen	2.0	2.0	1.7	0.02

Patient Ability to Communicate	75.2	68.0	67.7	0.02
Physician Ability to Communicate	94.9	90.2	90.9	0.03
Patient Ratings of Care	97.2	92.9	95.1	0.02

Table 2. Multiple Logistic Regression Analysis with Tamoxifen Use as the Outcome

Independent Variable	Standardized Coefficient	Odds Ratio (95% CI)
Age		
55 – 64	--Referent--	
65 – 74	0.21	2.2 (1.1, 4.4)
75 +	-0.01	1.0 (0.4, 2.6)
Physical Function	-0.2	0.98 (0.97, 0.99)
Stage	0.2	2.1 (1.1, 4.0)
Estrogen Receptor Status	0.41	5.6 (2.8, 11.2)
Standard Primary Therapy	-0.18	0.4 (0.2, 1.0)
Books/Magazines	-0.19	0.5 (0.3, 0.97)
Television Spots	0.15	2.1 (0.9, 4.9)
Number of Physicians	0.45	3.2 (2.0, 5.2)
Patient Ability to Communicate	0.24	2.8 (1.3, 6.1)

Table 3. Multiple Logistic Regression Analysis with Side Effects as the Outcome

Model A – Any Side Effects

Independent Variable	Standardized Coefficient	Odds Ratio (95% CI)
Age		
55-64	--Referent--	
65-74	-0.11	0.67 (0.3, 1.5)
75+	-0.25	0.31 (0.1, 0.9)
Education	0.12	1.9 (0.7, 5.5)
Emotional health	-0.31	0.97 (0.94, 0.99)
Stage	-0.12	0.7 (0.3, 1.4)
Estrogen Receptor Status	0.15	2.1 (0.8, 5.4)
Patient Ability to Communicate	0.1	1.5 (0.6, 3.7)
Model B – Hot Flashes		
Age		
55 – 64	--Referent--	
65 – 74	-0.18	0.5 (0.2, 1.2)
75+	-0.3	0.3 (0.1, 0.8)
Education	0.3	5.2 (1.3, 21)
Emotional Health	-0.35	0.96 (0.94, 0.99)
Stage	-0.16	0.6 (0.3, 1.2)
Estrogen Receptor Status	0.07	1.4 (0.5, 3.9)
Patient Ability to Communicate	0.03	1.1 (0.5, 2.6)

Table 4. Multiple Logistic Regression Analysis with Tamoxifen Discontinuation as the Outcome

Independent Variable	Standardized Coefficient	Odds Ratio (95% CI)
Age		
55 – 64	--Referent--	
65 – 74	0.05	1.2 (0.4, 3.4)
75+	-0.06	0.73 (0.1, 4.5)
Breast Cancer-related		
Standard Primary Therapy	-0.21	0.4 (0.1, 1.3)
Estrogen Receptor Status	-0.33	0.18 (0.1, 0.6)
Treatment Decision-making		
Books/Magazines	0.14	1.7 (0.6, 4.6)
Any Side Effects	0.36	4.0 (1.1, 13.9)

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